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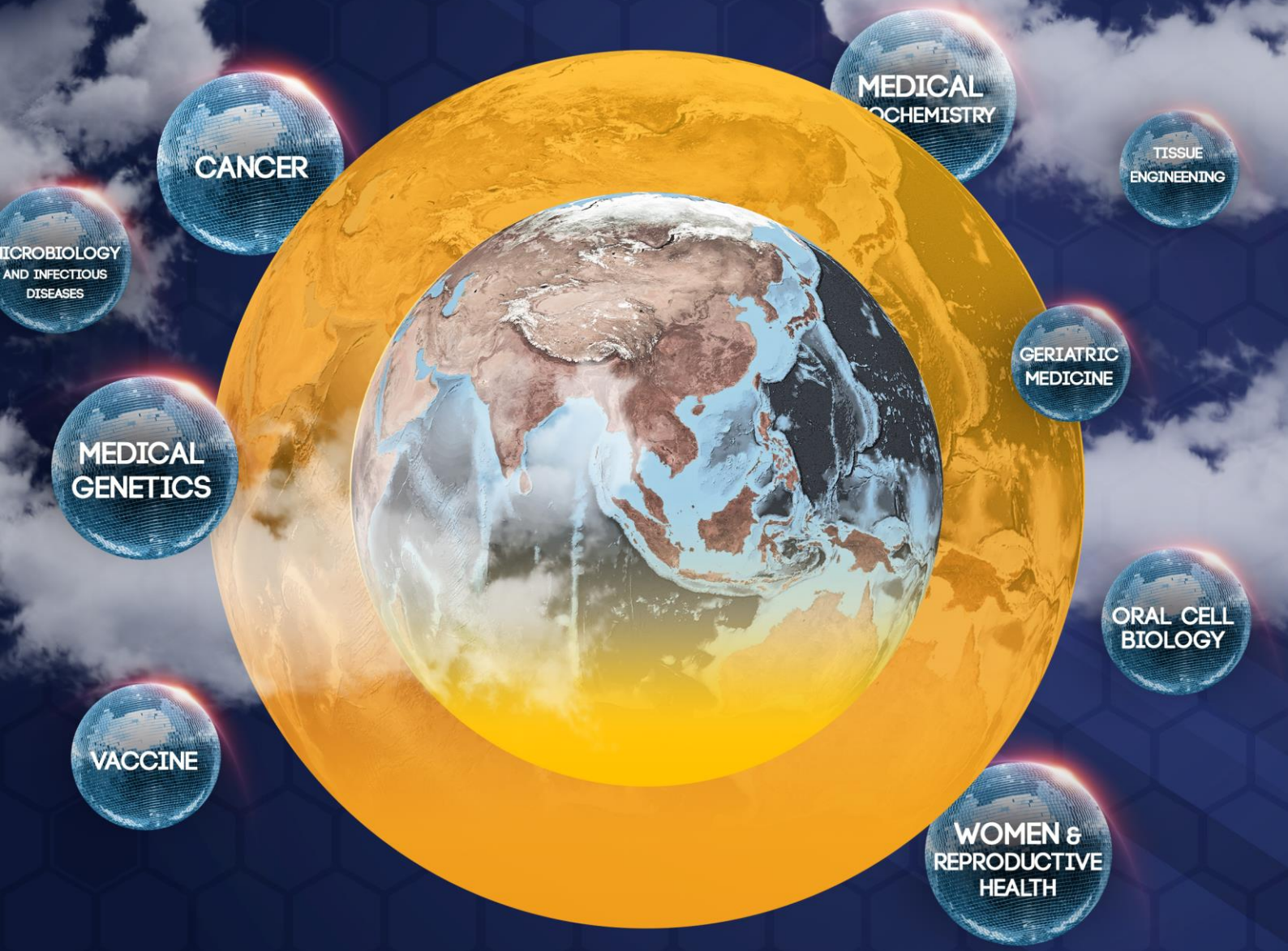

ICB 2023 Abstract Book

Includes a brief summary of keynote speeches and abstract of accepted articles.

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NEWTECH STUDIO

1. **17β-Estradiol-Loaded Exosomes for Targeted Drug Delivery in Osteoporosis: A Comparative Study of Two Loading Methods (Research Paper)**

Mohammad Sadegh Gholami Farashah,[1,*]

1. Tabriz University of Medical Sciences

Introduction: Exosomes are natural nanoparticles that participate in intercellular communication through molecular transport. Recently, due to their membrane vesicular structure and surface proteins, exosomes have been used extensively in the research field of drug delivery. Osteoporosis is an inflammation in which the cellular balance of bone tissue is disturbed that reduces bone density and making bone prone to abnormal fractures with small amount of force. Utilizing estrogen is one of the main therapeutic strategies for osteoporosis. Despite the positive effects of estrogen on bone tissue, changes in the natural estrogen levels of the body can cause a number of diseases such as different types of cancer. Therefore, designing a therapeutic system which controls more accurate tissue targeting of estrogen seems to be a rational and promising practical approach.

Methods: In this study, bone marrow mesenchymal stem cells (BMMSCs)-derived exosomes were loaded by estradiol using two different methods of drug loading, namely incubation and sonication methods and then the survival effects of the drug loaded exosomes on BMMSCs was investigated.

Results: Examination of size, shape, and surface factors of exosomes in different states (pure exosomes and drug loaded exosomes) showed that the round morphology of exosomes was preserved in all conditions. However, the particles size increased significantly when loaded by sonication method. The increased survival of BMMSCs was noted with estradiol-loaded exosomes when compared to the control group.

Conclusion: The results suggest that estradiol-loaded exosomes have potential to be used as nano-drug carriers in the treatment of osteoporosis.

Keywords: osteoporosis . exosome . drug delivery . 17β-estradiol . bone marrow mesenchymal stem cells

3D printing of PLA/PCL-Allograft Bone powder scaffold for bone tissue engineering application (Research Paper)

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4. Iranian Tissue Bank & Research Center, Gene, Cell, and Tissue Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Currently, over two million bone transplant surgeries are conducted globally on an annual basis. Addressing bone defects of significant size caused by tumors or trauma remains an unresolved requirement in the clinical field. Presently employed therapies involving xenografts, autografts, or allografts are burdened by several notable constraints, such as restricted availability, complications at the donor site, and the potential for disease transmission. Additionally, there exists a possibility of rejection by the body's immune system towards foreign materials. The process of surgically reconstructing bone tissue defects is both time-intensive and technically challenging. The desired outcome is not consistently attained, leading to patients experiencing lingering pain, lack of bone union, or infections resistant to treatment. Subsequently, a choice might be taken to proceed with a secondary amputation. Spatial printing, also known as 3D printing, involves creating tangible items using a computer-generated model. The utilization of 3D printing for bone grafts is increasingly significant and growing in popularity. The selection of the approach directly affects patient readiness for surgery, the likelihood of transplant rejection, and numerous other potential complications.

Methods: Allograft bone powders (BP) were introduced into acetone and subjected to 2 hours of sonication to yield a suspension containing 10 wt%. The suspension was combined with a PLAPCL solution in DCM, and then extensively mixed and ultrasonically dispersed for a duration of 2 hours. Ultimately, the PLAPCL-BP composite block was acquired once the solvent evaporated at ambient temperature. Fused deposition modeling (FDM) printers necessitate an original print material in the form of filament with a specific diameter. Therefore, converting the composite block into filament is

crucial. The composite block that was prepared underwent crushing using a mechanical crusher to yield composite powders. Subsequently, these powders were melted and extruded to generate filaments suitable for 3D printing. The object model was created using 3D modeling software (Solidworks, Dassault Systemes, France) and saved in the widely used STL format for 3D printing. Subsequently, the slicing software (Simplify 3D, America) was employed to determine the printing path. The morphology of all specimens was assessed using a scanning electron microscope (SEM; SU3500, Japan). Before observation, a gold sputter-coating was applied to all specimens. Subsequently, the SEM images were processed and the samples' pore sizes were measured using Image-J software.

Results: The PLA/PCL-BP scaffold could be efficiently printed using FDM technology. Furthermore, the printed scaffolds didn't need additional post-printing procedures (apart from rinsing and sterilization) before implantation, and they displayed appropriate mechanical and physical characteristics that allowed for additional handling. The micromorphology of the FDM-printed PLA/PCL-BP scaffold was examined using SEM. The figure revealed that all porous scaffolds exhibited a consistent macro structure, where filaments within the same layer ran in parallel, and adjoining layers intersected at a 90° angle. This printing approach resulted in the creation of a well-connected macroporous structure. The surface of the composite scaffold displayed noticeable exposed BP particles. Analysis through image processing with Image-J software indicated that the scaffold encompassed pores within the size range of 500-700 µm.

Conclusion: This study accomplished the successful fabrication of PLA/PCL-BP composite scaffolds featuring a substantial BP content through FDM 3D printing technology. This method, known for its affordability, convenience, and stability, facilitates the swift introduction of personalized bone repair biomaterials into clinical use.

Keywords: 3D printing; Bone grafts; Polylactic acid; Poly caprolactone; Scaffold.

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A Case Report of a Patient with Chondroplasia with Joint Dislocations , GPAPP type (Research Paper)

Faeze Khaghani,[1] Tayebeh Hamzehloei,[2,*]

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2. Dr Tayebeh Hamzehloei, Mashhad University of medical sciences, Genetics department, Mashhad-Iran.

Introduction: Chondroplasia with Joint dislocations , GPAPP type is a rare genetic disorder of the skeleton with autosomal ressesive inheritance which is caused by pathogenic mutations within the BPN2 gene. This gene encompasses 5 exons and encodes a golgi resident adenosine 3′, 5′-biphosphate 3′-phosphatase that contains 359 amino acids. This disorder is mainly characterized by short stature, joint dislocation, cleft palate, and hand anomalies such as brachydactyly.

Methods: DNA was extracted from whole bood in the case and his parents with soulthing out method. Primers were chosen for indinidual exons in the IMPAD1 gene and PCR were performed followed by DNA sequencing. The individual sequence was analyzed

Results: In this paper, we report a young male with short stature and hand malformations. He was the sixth and last offspring of a highly consanguine family with remarkable family history. His parents were first cousins and carried a pathogenic mutation (p.Asp 110 Glu) within IMPAD1 gene in a heterozygout state. The first child of the family was a girl who had similar symptoms and died at a young age. Then, the family aborted 4 following affected children. Genetic analysis was performed for this case and revealed a pathogenic mutation within the IMPAD1 gene in a homozygous state and confirmed the diagnosis

Conclusion: This study expands the genetic spectrum of chondroplasia with Joint dislocations condition.

Keywords: chondroplasia, IMPAD1 gene , autosomal recessive,

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A comparative assessment of RNF38 and P53 genes expression in the sperm samples obtained from males with normozoospermia and asthenospermia: A case-control study (Research Paper)

Alireza Alizadeh,[1] Sina Mirzaahmadi,[2,*] Golnaz Asaadi Tehrani,[3] Neda Jabbara,[4]

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Introduction: Background: Infertility is considered as a common problem appears in about 10-12% of couples in their reproductive ages. Ring finger protein 38 (RNF38) gene is a ubiquitin-protein ligase that can regulate Protein 53 (P53) and affect cellular motility. Objective: Considering the role of P53 on cellular motility and RNF38 on the regulation of P53, the present study aimed to assess the difference between RNF38 and P53 genes expression in normozoospermic and asthenospermic samples as a diagnostic biomarker in males.

Methods: Materials and Methods: The present study was conducted among 21 asthenospermics and 63 healthy individuals. First, the real-time polymerase chain reaction technique was applied to measure the expression level of the P53 and RNF38 genes extracted from sperm samples, and the glyceraldehyde-3phosphate dehydrogenase gene was selected as the reference gene.

Results: Results: An increase and a decrease occurred in the level of P53 and RNF38 genes expressions in asthenospermic and normozoospermic samples, respectively. In addition, a significant difference was observed between increasing P53 gene expression ($p < 0.001$), reducing RNF38 one, and decreasing sperm motility ($p < 0.001$) in asthenospermic cells compared to that of normozoospermic ones.

Conclusion: Conclusion: Based on the results, an increase in the expression of the P53 gene and a decrease in the expression of the RNF38 gene had a significant relationship with asthenospermia in men. Therefore, it is expected that an effective step should be adopted to diagnose the asthenospermia expression pattern by using these results.

Keywords: RNF38, P53, SDFA, Real time-PCR, Normosperm, Asthenosperm

A comparative study of the effects of Atorvastatin, Simvastatin, Atorvastatin and Lovastatin on SLCO1B1, using molecular docking methods. (Research Paper)

Bahar Akbari,[1,*]

1. IAU, medical sciences, Tehran branch

Introduction: Drug discovery and molecular docking is a challenging process, and identifying the right lead compound is a determining factor in the overall success of the project. This paper discusses the process of drug discovery and molecular docking, which is a challenging process. The paper focuses on identifying the right lead compound, which is a determining factor in the overall success of drug discovery. The study compares the effects of Atorvastatin, Simvastatin, and Lovastatin on SLCO1B1 using molecular docking methods. SLCO1B1 is a protein found in humans that belongs to the solute carrier organic anion transporter family. It transports various types of organic anions, conjugated steroids, eicosanoids, and thyroid hormones. The wide range of compounds transported by SLCO1B1 suggests it plays an important role in the clearance of endogenous and exogenous substances from the liver and other tissues. The pH sensitivity of SLCO1B1 towards certain compounds suggests that the binding site of the protein may be affected by the acidity of the surrounding environment, which could have implications for its function in different tissues. Atorvastatin (ATV) is a medication used to lower cholesterol and lipid levels in the blood, reducing the risk of cardiovascular disease. It belongs to the statin class of medications and works by inhibiting the endogenous production of cholesterol in the liver. Statins are the most commonly prescribed medication for treating abnormal lipid levels. ATV is transported in the blood almost exclusively bound to plasma proteins and is subject to pre-systemic clearance at the gastrointestinal tract and to first-pass hepatic clearance, which explains its low systemic bioavailability. Elimination of ATV and its metabolites is principally biliary, with no significant enterohepatic recirculation. Simvastatin is a medication derived from Aspergillus terreus and is used to lower the risk of cardiovascular disease by inhibiting cholesterol production. It belongs to the statin class of medications, which inhibits the enzyme HMG-CoA Reductase involved in producing of cholesterol and other lipid compounds. Statins, including simvastatin, atorvastatin, and lovastatin, are widely prescribed due to their proven benefits and minimal side effects. Elevated cholesterol levels, especially LDL levels, are a significant risk factor for CVD, and statins have been shown to effectively reduce this risk. Statins are cost-effective and beneficial even for low-risk individuals, as they can significantly reduce the

occurrence of major cardiovascular events without significant side effects. Lovastatin is a medication derived from a fermentation product of Aspergillus terreus and belongs to the statin class of medications. It is used to lower the risk of cardiovascular disease by inhibiting the production of cholesterol in the liver. Statins, including lovastatin, competitively inhibit the enzyme HMG-CoA Reductase, which is involved in producing cholesterol and other lipid compounds. Statins are widely prescribed due to their proven benefits and minimal side effects. Elevated cholesterol levels, especially low-density lipoprotein (LDL) levels, are a significant risk factor for CVD. Statins have been proven to effectively lower LDL levels and reduce the risk of CVD and all-cause mortality, even in low-risk individuals. Rosuvastatin is the most potent statin medication, while lovastatin has a lower average decrease; however, clinical outcomes between statins show minimal differences.

Methods: For the preparation of the macromolecule, we use websites such as Uniprot to extract the 3d structure of our protein. The most suitable protein structure is one with a high resolution, less chains and a higher amount of nucleotides. The best format for saving the protein is PDB After finding the 3d structure, we open the protein in UCSF Chimera, for the purposes of deleting the unwanted chains, side-chains, etc. Then we will prepare it for docking by going to the tools menu and clicking Surface/Binding Analysis - Dock Prep. We have used chain A of the protein SLCO1B1. For the preparation of the ligand- drug-, we first download the suitable drugs using websites such as PubChem. Then we will download the ligands 3d structure with the SDF format. We usd the drugs Lovastatin, Simvastatin and Atorvastatin. Both the ligand and the receptor are opened in PyRx. PyRx is a Virtual Screening software for Computational Drug Discovery that can be used to screen libraries of compounds against potential drug targets. First, the ligands and the receptor are opened in PyRx. Then we will select the perfect site action for the ligands. After this selection, the software will start docking.

Results: The results will be shown below the screen after the docking is done. In the case of the binding affinity, the more negative the numbers, the better the result. RMSD lower and upper bonds should also be zero, for a good result. Binding affinities of atorvastatin, simvastatin and lovastatin are as follows: -8.4, -7.9, -7.6

Conclusion: Among the mentioned drugs, atorvastatin is the most effective for SLCO1B1 protein malfunction illnesses.

Keywords: SLCO1B1, Molecular docking, Atorvastatin, Simvastatin , Lovastatin

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A comparison between centrally and systemically administered erythropoietin on kidney protection in a model of fxed-volume hemorrhagic shock in male rats (Research Paper)

Mina Ranjbaran,[1] Mehri Kadkhodaee,[2] · Maryam Adelipour,[3] · Leila Hafazeh,[4] Keivan Lorian,[5] Behjat Seif,[6,*]

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5. Research and clinical center for infertility, Yazd Rreproductive Sciences Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
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Introduction: In this study, a comparison between centrally and systemically administered erythropoietin (EPO) was per formed on nephroprotection during hemorrhagic shock (HS) in mal

Methods: s Male rats were allocated into four experimental groups. (1) Sham; a guide cannula was inserted into the left lateral ventricle and other cannulas were placed into the left femoral artery and vein. (2) HS; stereotaxic surgery was done to insert a cannula in the left lateral ventricle and after a 7-day recovery; hemorrhagic shock and resuscitation were performed. (3) EPO-systemic; the procedure was the same as the HS group except that animals received 300 IU/kg erythropoietin into the femoral vein immediately before resuscitation. (4) EPO-central; animals was treated with erythropoietin (2 IU/rat) into the left lateral ventricle before resuscitation. Arterial oxygen saturation (SaO2) was measured during experiments. Urine and renal tissue samples were stored for ex-vivo indices assessments.

Results: Erythropoietin (systemically/centrally administered) signifcantly improved SaO2, renal functional and oxidative stress parameters and decreased renal infammatory (TNF-α and IL-6) mRNA expression compared to the HS group. EPO-treated groups showed a decrease in active form of caspase-3 protein level and an increase in autophagy activity in comparison with the HS group.

Conclusion: Considering the fact that the efective dose of systemic EPO (300 IU/kg) was roughly 50 times higher than that of central administration (2 IU/rat), centrally administered EPO was accompanied by more advantageous consequences than systemic way. EPO is likely to act as a neuro-modulator or neuro-mediator in the central protection of organs including the kidneys

Keywords: Erythropoietin · Hemorrhagic shock · Inflammation · Intracerebroventricular infusion · Stereotaxic

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A COMPARISON BETWEEN LABLOTARY FERTILIZATION AND EGG DONATION: ASSISSTEND REPRODUCTIVES TECHNIQUE IN WOMEN WHTH ENDOMETRIOSIS (Review)

Reyhane Bahrami,[1,*]

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Introduction: Endometriosis distorts pelvic function and anatomy through adhesions which could be associated with disorders in ovulation, fertilization and implantation in women with this problem. Recent advances in assisted reproductive techniques including artificial insemination and egg donation have increased the likelihood of childbearing for women with endometriosis who wish to have children. The present study was conducted to compare between laboratory fertilization and egg donation in women with endometriosis.

Methods: Methods: This systematic review was performed in Medline, EMBASE, Cochrane library, Science direct and Springer databases to find relevant articles. Search terms included lab oratory insemination, egg donation and endometriosis. Cohort studies (prospective and retrospective , case-control and case report studies assessing the results of egg donation and laboratory fertilization techniques in infertility among women with endometriosis were included. Out of52 papers identified through initial search, 40 relevant studies were selected from which, 19 paper s were included in this systematic review.

Results: Results: As compared to egg donation, rate of fertility and implantation were lower in laboratory fertilization per each cycle of using this technique in women with endometriosis (after 3 course of treatment, 48% v 58%). A direct association was observed between age of egg donor, egg quality, number of transferred fetuses to the uterus with implantation and live birth pregnancies ($p<0.05$).

Conclusion: Conclusion :It seems that egg donation method could be among acceptable approaches in order for infertility treatment among women with endometriosis.

Keywords: Assisted reproductive techniques, laboratory fertilization, egg donation, endometriosis

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A Comprehensive Review of Multilayer Structures for Enhanced Wound Recovery (Review)

Samin Hamidi,[1,*]

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Introduction: Multilayer platforms have emerged as promising tools in the field of wound healing, offering a multifaceted approach to promote effective and accelerated tissue regeneration. This review article aims to provide a comprehensive overview of the various multilayer platforms employed in wound healing applications, highlighting their structure, fabrication methods, and potential mechanisms of action.

Methods: The first section of the review focuses on the design and composition of multilayer platforms, encompassing different materials such as polymers, hydrogels, and biocompatible scaffolds. It discusses the significance of each layer in terms of its specific functionalities, including cell adhesion, drug/bioactive factor loading, antimicrobial properties, and mechanical support. The second section of the review delves into the mechanisms of action associated with multilayer platforms in wound healing. It discusses how these platforms facilitate wound closure, promote angiogenesis, modulate inflammation, and enhance tissue regeneration. The article also examines the role of multilayer platforms in providing a physical barrier against external pathogens, reducing the risk of infection, and creating a favorable microenvironment for wound healing.

Results: Multilayer wound dressing platforms offer significant potential in enhancing outcomes in the management of both acute and chronic wounds. They represent a captivating avenue for achieving improved outcomes in the realm of wound healing.

Conclusion: Overall, this review highlights the significant advancements made in the field of multilayer platforms for wound healing and underscores their potential as versatile therapeutic strategies.

Keywords: Advanced wound care, Bioengineering, Multilayer platforms, Wound healing

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A comprehensive review of the clinical findings of shiga toxin-induced HUS (Review)

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Introduction: HUS , disease that with triad of features thrombocytopenia, hemolytic anemia, and ischemic organ damage characterized. It is caused by gastrointestinal infection by a Shiga toxin-producing E.coli (and occasionally other pathogens). Functionally, the Shiga toxins belong to the family of ribosome-inactivating proteins. The O104:H4 sero type E.Coli stands out as one of the most virulent strains responsible for HUS and The O26:H11 serotype has emerged as the most common non-O157 serotype causing human disease. Route of transmission is mostly foodborne.

Methods: was conducted using the PubMed/MEDLINE , EMBASE databases using search terms "HUS" , “STEC" , “shiga toxin " Search restrictions included the English language and full text availability. A total of 42 articles were identified, and 25articles remained after removing duplications. Abstracts were screened for pertinent information.

Results: STEC-HUS is one of the most common diseases requiring emergency renal replacement therapy in children and is responsible for 2%–5% of mortality worldwide during the acute phase. Approximately 5%–10% of infected patients will develop STEC-HUS about a week after the onset of digestive signs. Rural areas also tend to be more affected than urban ones, and cases occur predominantly during summer months. age is also an important risk factor for HUS and also reported that female sex and a higher socio-economic status are associated with a higher risk of developing STEC-related disease. Gastric acidity is an important barrier to ingested pathogens. Hypochlorhydria, whether related to gastrectomy or to proton pump inhibitors, has been associated with an increased risk of STEC infection and STEC-HUS. Genetic factors, like erythrocyte and serum Gb3 level or presence of the platelet glycoprotein 1b alpha, could also influence the susceptibility to HUS. The presence of the intimin (eae) gene is associated with human disease and evolution towards hemorrhagic colitis and HUS. In any case, the estimated half-life of shiga toxin in serum is less than 5 min, as it rapidly diffuses to affected tissues. It is thus likely that by the time patients develop HUS, shiga

toxin has disappeared from the serum. STEC-related diseases display a wide range of severity, from asymptomatic carriage to lethal HUS. STEC-HUS mainly occurs through large outbreaks. The disease being usually limited to the colon and not prone to bacteremia. STEC-HUS does not usually recur. The kidneys bear the brunt of most of the long-term sequelae. Need and duration of dialysis are seemingly the most reliable predictors of poor renal outcome. Next to renal sequelae, central nervous system involvement is one of the most dreaded complications of STEC-HUS. It is responsible for the majority of patient deaths and is an important contributor to the morbidity of the disease. For patients with renal sequelae after STEC-HUS, a low-sodium diet, early restriction of protein intake, seem to slow down the progression of chronic kidney disease.

Conclusion: Over 30 years after the description of Shiga toxins and Shiga toxin E. coli-associated HUS , the quest for a specific treatment remains elusive, despite major achievements in the understanding of the pathophysiology of the disease, and the encouraging results in preclinical models and ongoing clinical trials, a specific treatment is still absent. Supportive therapy is the cornerstone of the treatment of STEC-HUS patients.

Keywords: STEC-HUS, hemorrhagic colitis, renal sequelae, treatment, bacteremia

A G-quadruplex aptamer for electrochemical sensing of 25-Hydroxy vitamin D3 based on CuCo2O4/N-CNTs nanocomposite (Research Paper)

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4. Metabolic Syndrome Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
5. Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
6. Medical Genetics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: The measurement of serum 25-hydroxyvitamin D3 (25(OH)D3) levels is essential because of its significant role in immune function and bone metabolism as well as the relationship between its deficiency and complications such as neurodegenerative, depression, cancer, diabetes, and cardiovascular diseases. This study describes a novel electrochemical aptasensor based on a rationally truncated aptamer for sensitive, selective and low-cost quantification of 25(OH)D3.

Methods: The aptasensor contains a glassy carbon electrode modified with CuCo2O4/N-CNTs nanocomposite and an engineered aptamer. Three new aptamers (VDBA14-23, VDBA14-27, and VDBA14-35) were designed via truncation of the previously selected DNA aptamer (VDBA14, 56-mer). The sensitivity and selectivity of VDBA14 and new truncated aptamers toward 25(OH)D3 were studied through the differential pulse voltammetry technique. Introducing 25(OH)D3 changes the flexibility and conformation of the aptemers and the detection strategy is done based on the peak current intensity of the redox marker [Fe(CN)6]3-/4-.

Results: In the DPV tests, the sensors built with the G-quadruplex VDBA14-35 aptamer showed improved sensitivity and specificity toward 25(OH)D3 than the parent VDBA14. Under optimized experimental conditions, the aptasensor response decreases with increasing the concentration of

25(OH)D3 and is linear with the logarithm of 25(OH)D3 concentration in the range from 1×10-13 to 1×10-6 M. The detection limit of the VDBA14-35/CuCo2O4/N-CNTs/GCE sensing is 0.063 pM (based on 3Sb/m).

Conclusion: The fabricated aptasensor is simple, low-cost, selective, and sensitive. This sensor would be of great benefit for the clinical diagnosis of 25(OH)D3.

Keywords: Truncated aptamer, Biosensor, Vitamin D, Tertiary structure.

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A genetic risk called breast cancer (Review)

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Introduction: Breast cancer is one of the most common cancers among women. In the last four decades, the incidence of this cancer has increased rapidly, and this value increases by 0.5% every year. But fortunately, the death rate due to breast cancer has been decreasing since its peak (1989) and we owe this decrease to early diagnosis and prevention methods in many cases.

Methods: To write this article, the Google scholar database was used, and in this search, using the advanced search feature, we set a limited date between 2019 and 2023. Searched terms included breast cancer, genes of breast cancer, cancer diagnosis, breast cancer prevention methods, breast cancer statistics, breast cancer treatment.

Results: Breast cancer starts when breast cells grow out of control. A large number of breast cancer diagnoses are made through a mammogram (an X-ray scan). Breast cancer diagnosis is also done by touching an abnormal mass by the person or doctor concerned. At the time of diagnosis, the cancer cells may be only in the breast tissue or it may have migrated to the armpit lymph nodes or distant places, and based on the location of the cancer gland, breast cancer has stages 1 to 4; the fourth stage is called metastatic cancer. Risk factors for breast cancer: • Genetic factors: The most common genes in causing breast cancer are BRCA1 and BRCA2, which are involved in the repair of DNA double-strand breaks, which account for about 2.5% of all inherited breast cancer mutations. Other breast cancer causative genes with high and moderate penetrance include cadherin 1 (CDH1), PTEN, protein serine/threonine kinase 11 (STK11), TP53, CHEK2, ataxia telangiectasia mutated (ATM), nibrin (NBN), which may All these genes are associated with BRCA2. Non-genetic factors: Other risk factors include high body mass index, early menarche (before age 13), first delivery over age 30, family history of breast or ovarian cancer, late menopause and postmenopausal hormone therapy, exposure to chest x-rays. , obesity and alcohol, insufficient physical activity and short breastfeeding period. Symptoms of breast cancer: The presence of a palpable mass in about 30% of women, indentation, orange skin appearance, edema, blisters, cuts, secretions from the nipple, nipple shrinkage, and in advanced cases, ulcers are observed. Of course, a palpable

mass is also possible in benign conditions. There is a patient referred for diagnosis. Breast cancer diagnosis: After the clinical examination, basic imaging methods including mammography and ultrasound are used for diagnosis. Certain conditions such as dense tissue in the breast, history of breast cancer, history of breast surgery or radiation therapy are used for MRI. To confirm the presence of cancerous tissue, biopsy or needle sampling is performed under the guidance of ultrasound or MRI. Sometimes a piece of the lump in the breast is removed by surgery and sent to pathology for a definitive diagnosis. Prevention of breast cancer: Screening for risk genes and genetic counseling for mutation carriers is a suitable prevention method. Monthly breast and armpit examinations, mammography from the age of 35 years and above, ultrasound and reducing exposure to non-genetic risk factors such as proper physical activity, weight control, no alcohol consumption, birth of the first child at a younger age, no additional hormone therapy after menopause.

Conclusion: Considering the side effects of cancer and its role in reducing the quality of life of women and increasing their mortality rate, as well as the high costs of treatment, the role of preventing the occurrence of the disease becomes very important. In this article, we found a correct understanding of genetic factors in the development of breast cancer, which can prevent the disease in a significant number of women by performing genetic tests and genetic counseling.

Keywords: breast cancer cancer Genetics prevention

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A glance at cancer vaccines (Review)

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Introduction: Cancer is an important issue globally that leads to death and its mortality rates are increasing in worldwide. In recent years, cancer vaccines are considered as a promising immunotherapy development and used in two ways: 1. Preventive vaccines 2. Therapeutic vaccines. Preventive vaccines can prevent cancers caused by viruses such as hepatitis B and human papilloma through inducing immune memory. However, these types of vaccines cannot be used for all types of cancer, because all of them are not caused by viruses. Cancer therapeutic vaccines are designed and can applied for stimulation tumor regression, eradication minimal residual signs of illness, build up enduring antitumor memory and prevention of some non-specific or also harmful reactions.

Methods: In this study, 6 articles were selected from the Scopus search database based on keywords including cancer, vaccine and immune system from 2020-2022

Results: Selecting the appropriate antigen is very significant for vaccine design. Tumor antigens can be divided into two notable categories: 1. Tumor associated antigens (TAA) that are expressed in malignant or non-malignant tissues and are categorized into three types: overexpressed antigens, cancer testis antigens, and differentiated antigens. 2. Tumor specific antigens (TSA) that are expressed only in tumor cells and are sometimes called neoantigens. TSAs have stronger immunogenicity and greater affinity to MHCs compared TAAs, and cause the appropriate response of tumor specific T cells with less damage. Recently, they are the notable target of cancer vaccine design. Based on different preparation methods, The platform of cancer vaccines are categorized into 4 groups: cell-based vaccines, virus-based vaccines, peptide-based vaccines, and nucleic acid-based vaccines. After tumor vaccine administration, dendritic cells (DCs) take up and process tumor antigens. Subsequently, their migration to the lymph nodes occurred resulting in recruiting activating of immune cells. DCs activate CD4+ and CD8+ T cells through presenting tumor processed antigens to major histocompatibility complex II (MHCII) and MHCI, respectively. Finally, T cells differentiation

occurs and divided them into effector and memory T cells. Activation of these cells leads to proliferate and differentiate of CD8+ T cells into cytotoxic T lymphocytes (CTLs). These cells destroy tumor cells through the production of compounds such as perforin and granzyme and the interactions of Fas and FasL. In addition, CTLs can inhibit the angiogenesis of tumor cells by producing IFNγ. Moreover, CD4+ T cells control and also support the differentiation and effective responses of CD8+ T cells through producing IFNγ. Furthermore, CD4+ T cells with follicular DCs differentiate B cells into memory B cells and plasma cells and activation of B cells results in tumor cell apoptosis by antibody-dependents cell cytotoxicity (ADCC).

Conclusion: Immunotherapy and cancer vaccines are promising therapeutic methods to eliminate tumor cells. However, more studies are needed to identify suitable antigens and develop cancer vaccines which lead to effective and common treatment for cancer

Keywords: cancer, vaccine, immune system, immunotherapy, tumor

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A micelle-hydrogel composite for the delivery of growth factors in regenerative diseases (Research Paper)

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Introduction: Anosmia is the inability to smell or loss of the sense of smell. It can reduce your ability to detect the smell of smoke, gas leaks, or spoiled food, as well as hinder the quality of life related to social interactions and feelings of well-being. In the current study, a drug delivery composite was designed to cure anosmia and its efficiency in delivering transforming growth factor alpha (TGF-α) and transforming growth factor beta 1 (TGF-β1) to the nasal cavity was evaluated. Bovine serum albumin (BSA) was used as a model protein for encapsulation into Poloxamers 407 micelles. For the optimization of the BSA-micelle formulation, a two-parameter five-level central composite design (CCD) was applied. The BSA-micelle was optimized with a particle size of 41 nm, drug loading of 8%, and _encapsulation efficiency of 74%_. Further, the BSA-micelle was characterized by FESEM, TEM, and FTIR. The analysis of release profile suggested high-paced free BSA release compared to the gradual and prolonged release of BSA-micelle/hydrogel and BSA-micelles. The cytotoxicity assay demonstrated the safety of TGF-α and TGF-β1-micelles/hydrogel. Moreover, it was observed that TGF-α and TGF-β1 within the hydrogels promote cellular viability and human olfactory ectomesenchymal stem cell OE-MSCs proliferation. In conclusion, According to the results of our study, the TGF-α and TGF-β1-micelle/hydrogel-based delivery system provides a suitable alternative for anosmia treatment..

Methods:

Results:

Conclusion: ,

Keywords: Anosmia, Poloxamer, Olfactory disorder, Growth Factors, Regenerative diseases

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A Microarray Profile of Triple Negative Breast Cancer related to onco-miRNAs and Their Target Genes (Research Paper)

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Introduction: Triple negative breast cancer (TNBC), a subtype of breast cancer characterized by its aggressive nature, has higher lethality rates in affected women among other types of breast cancer. It has been shown that microRNAs (miRs) are associated with the progression of TNBC, since these molecules can affect the expression levels of their target genes and control specific pathways as a result. Here we focused on detecting dysregulation of miRs and their target genes in TNBC.

Methods: First, the gene expression omnibus (GEO) database was searched for microarray studies using TNBC samples and control samples. We searched for datasets that employed the miR and mRNA platforms in their research designs. After data analysis based on the limma packages methodology, the second step involved the discovery of deregulated miRs and mRNAs using the web program GEO2R. The filter for determining the differentially expressed miRs/mRNAs (DEMs/DEGs) was applied (|logFC| > 2 and pvalue < 0.5), and only up regulated DEMs were selected for further target gene detection using bioinformatics analysis. Thirdly, only down regulated DEGs that were also in common with the predicted target genes of the DEMs were selected for pathway detection, gene ontology (GO) and protein network analyses as well as expression validation on UALCAN data base.

Results: One miR related microarray study (GSE154255) and two microarray studies using gene expression profiling platforms (GSE113865 and GSE65216) have entered in this study. Following the filtration, the GSE154255 included 33 DEMs with 9 miRs that were up expressed and 23 miRs that were downregulated. The target genes of all the 9 upregulated DEMs (hsa-miR-590-5p, hsa-miR-182-5p, hsa-miR-183-5p, hsa-miR-18a-5p, hsa-miR-18b-5p, hsa-miR-491-3p, hsa-miR-362-3p, hsa-miR-301a-3p and hsa-miR-7-5p) that were matched with the list of down expressed mRNAs in TNBC microarray datasets contained 2755 genes in total. The MAPK

signaling pathway was the one that was most substantially enriched in TNBC, according to KEGG pathway analysis.

Conclusion: Altogether, through using an in silico method, this study showed hsa-miR-590-5p, hsa-miR-182-5p and hsa-miR-18b-5p had the highest expression levels in TNBC samples.

Keywords: Triple negative breast cancer, Gene expression omnibus, microRNAs, microarray, bioinformatics

A network-based approach to identify hub genes in Huntington's disease (Research Paper)

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Introduction: Huntington's disease (HD) is a rare neurodegenerative disease characterized by progressive degeneration of neurons in the cerebral cortex and basal ganglia. HD is an autosomal dominant disorder caused by the expansion of CAG trinucleotide repeat in the Huntingtin gene (HTT) and defined by cognitive, psychiatric and motor disturbance. Although HD has been shown to have a genetic origin, its underlying cellular and molecular mechanisms are still not well understood and remain unclear to date. Therefore, early detection of HD by specific biomarkers can lead to earlier initiation of treatment programs, lifestyle modification and increase the patient's quality of life. Hence, this study was designed to identify the key genes and related pathways in HD.

Methods: The gene expression omnibus (GEO) available at https://www.ncbi.nlm.nih.gov/geo was used to obtain the gene expression profile of Huntington's disease (GSE1751) including 12 HD samples and 14 control samples. Screening and analysis of differentially expressed genes (DEGs) between HD and healthy controls were performed using R programming language. Genes with p-value < 0.05 and |logFC| ≥ 1.0 were considered as DEGs. The enrichment analysis of HD-related genes was performed by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway using Enrichr (https://maayanlab.cloud/Enrichr). Additionally, the Search Tool for the Retrieval of Interacting Genes (STRING) database (http://string-db.org/) was used to predict protein–protein interactions (PPI) network of identified DEGs. The PPI network visualization and analysis were employed using Cytoscape 3.9.0. The plug-in CytoHubba and degree centrality were applied to select 10 hub genes. MCODE was also used to distinguish top structural modules in the PPI network.

Results: In general, 404 genes were up-regulated and 1492 genes were down-regulated. GO biological process showed that DEGs are associated with proteasome-mediated ubiquitin-dependent protein catabolic process, cotranslational protein targeting to membrane, cytoplasmic translation, regulation of apoptotic process, and protein targeting to ER. GO Molecular function indicated a relationship between DEGs and RNA binding, nuclear receptor binding, cadherin binding, alpha-amylase activity, and nuclear import

signal receptor activity. GO cellular components revealed that DEGs are related to intracellular membrane-bounded organelle, COPII-coated ER to Golgi transport vesicle, bounding membrane of organelle, cytoplasmic vesicle membrane, and nuclear inner membrane. KEGG pathway enrichment analysis demonstrated a relationship of DEGs with Coronavirus disease, Autophagy, Th17 cell differentiation, Ubiquitin mediated proteolysis, Pathways in cancer, Lipid and atherosclerosis, and Ribosome. A total of 1554 nodes and 14888 edges were involved in the PPI network. Based on degree, 10 genes including HSP90AA1, PTEN, JUN, HIST1H4F, SIRT1, FN1, SMARCA4, SUMO1, CASP3, and SRSF1 were referred as hub genes.

Conclusion: Based on key modules related to HD, PTEN, HIST1H4F, SIRT1, FN1, and SMARCA4 genes may have potential value in detecting and predicting HD progression. More experimental validations are needed for better understanding the role of these genes in HD.

Keywords: Huntington's disease, HD, Network-based analysis, Systems biology, Biomarker

A new approach to reversing resistance to therapies by targeting cancer stem cells: signaling , mechanisms, and potential agents (Review)

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Introduction: The ability of cancer stem cells (CSCs) to self-renew and differentiate is an important factor that contributes to tumor progression and resistance to therapies. In spite of this, it remains unclear as to how the underlying processes work. By understanding the key characteristics and the mechanism of resistance of CSCs, it may be possible to improve patient outcomes and reduce the likelihood of relapse in the future. A clinical perspective was presented in this review, which highlights CSC identification, intrinsic and extrinsic mechanisms of therapy resistance within CSCs, signaling pathways within CSCs that contribute to loss of responsiveness to treatment, along with possible CSC-targeting agents for various types of cancer.

Methods: There was an extensive research effort conducted between the years 2000 and 2020 to target cancer stem cells and address the issue of therapy resistance in the treatment of cancer. The aim of this study is to retrieve pertinent studies that have been published during the period of time under discussion, by searching reputable databases such as Scopus, PubMed, Science Direct, and Google Scholar. As part of the search strategy, we aimed at identifying literature located on mechanisms, potential agents and signaling pathways that may be able to reverse therapy resistance in CSCs using their mechanisms and signaling pathways. A particular set of keywords were used to identify the research, which included "cancer stem cells," "therapy resistance mechanisms," "signaling pathways in CSCs," and "novel therapeutic agents." The original 10,000 studies that were identified were screened based on abstracts, with 9700 being excluded based on abstracts, leaving 300 studies for review in full. In order to perform a

comprehensive review of all the articles that were considered relevant to this study, a rigorous screening process was conducted. The objective of this study was to shed light on the complex mechanisms that underlie therapy resistance in CSCs and identify potential agents that might provide new approaches to the treatment of cancer.

Results: There are a variety of types of cancer that can be treated by targeting their cancer stem cells in order to overcome therapy resistance. Throughout the past few years, there has been an increasing focus on identifying potential agents that can reduce CSC resistance, as well as unraveling the signaling pathways involved in CSC-driven resistance. The results of this study have shown that CSCs play a critical role in the resistance to treatment as a result of this study. There is growing evidence to suggest that CSCs can survive conventional cancer treatments due to their self-renewal ability and multidrug resistance. As a result, conventional cancer treatments fail. A number of key mechanisms have been discovered by researchers over the last few years. It has been demonstrated that several signaling pathways play a role in regulating the maintenance and resistance of CSCs, including Notch, Wnt, and Hedgehog. Several studies have shown that targeting these pathways is effective in stimulating the response of CSCs to therapy when they are targeted. There have been many compounds tested in preclinical and clinical trials in order to determine if they could serve as potential agents in the future. Inhibitors of small molecule receptors, monoclonal antibodies, and natural compounds have been shown to be effective in selectively targeting CSCs. Several preclinical studies have shown that CD44 inhibitors, ALDH inhibitors, and specific kinase inhibitors have demonstrated encouraging results in preclinical studies.

Conclusion: A better understanding of the mechanisms underlying CSC-mediated resistance to therapy, as well as the identification of potential agents that can target CSCs, is crucial to improve cancer treatment outcomes and overcome resistance difficulties. It is imperative to build an understanding of the mechanisms that underlie CSC-mediated resistance to therapy. There is promise in these efforts for enhancing the efficacy of future cancer therapies.

Keywords: Cancer stem cells Resistance potential agent mechanism cancer treatment

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A Novel Homozygous Frameshift Insertion Mutation in The RPE65 Gene Causes Autosomal Recessive Retinitis Pigmentosa (Research Paper)

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Introduction: Retinitis pigmentosa (RP) is a group of hereditary deteriorations illustrated by progressive dysfunction of primarily rod photoreceptors followed by cone ones. RP without correlated systemic disease known as Typical RP has an estimated prevalence of 1:4000 globally. Patients developed typical RP manifest in the first or second decade of life with night blindness, progressive loss of the peripheral visual field followed by the loss of central vision, and final total blindness. Different inheritance patterns comprise autosomal dominant, autosomal recessive, and X-linked. Studies have reported at least 50 distinct genes to be related to RP. In this study, peripheral blood sample from patient with retinitis pigmentosa (RP), Whole-exome sequencing (WES) data, and Sanger sequencing data were integrated to assess the causing mutation of retinitis pigmentosa (RP) in an Iranian family.

Methods: Whole-exome sequencing (WES) performed on proband to screen pathogenic mutations and also Sanger sequencing performed on family members in order to confirm whether the detected mutation was related to the disease.

Results: This research demonstrated a significant frameshift insertion mutation that inherited from heterozygous unaffected carriers to affected individuals as a homozygous frameshift insertion mutation in the retinal pigment epithelium-specific 65 kDa protein (RPE65) gene (NM_000329: exon9: c.886dupA: p.R296fs). Therefore, this mutation has been identified as the cause of autosomal recessive retinitis pigmentosa (ARRP).

Conclusion: In conclusion, homozygous frameshift insertion mutation (NM_000329: c.886dupA: p.R296fs) in exon9 of RPE65 also known as retinoid isomerohydrolase is reported as the genetic cause of retinitis pigmentosa for the first time.

Keywords: Autosomal recessive retinitis pigmentosa, RPE65, whole-exome sequencing, sanger sequencing

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A Preliminary Study: Effect of nanomicelle curcumin on sperm function in varicocele patient (Research Paper)

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Introduction: Varicocele is one of the most important causes of infertility in men which gradually leads to testicular dysfunction. Testicular heat stress-induced oxidative stress is considered the main cause of pathology in these individuals. In this study, the effects of nanomicelle curcumin, as natural antioxidants, were investigated on spermatogenesis and sperm function in varicocele patients.

Methods: This prospective clinical trial included 35 infertile men with varicocele randomly divided into control (n=20) and nanomicelle curcumin (n=15) groups. We assessed semen parameters, DNA integrity [terminal deoxynucleotidyltransferase-mediated dUTP nick-end labeling (TUNEL)] and oxidative stress factors (total antioxidant capacity, Malondialdehyde) at the baseline and at the end of the study.

Results: At the end of study, statistically significant differences were seen in the sperm concentration, motility, and normal morphology in the intervention group to the control group($p<0.05$). In treatment group, the sperm concentration, motility, and normal morphology levels were also statistically increased at the end of study compared to the baseline values($p<0.05$). Nanomicelle curcumin supplementation also resulted in a statistically significant improvement in DNA integrity, plasma levels of total antioxidant capacity, and Malondialdehyde in comparison to the control group ($p<0.05$).

Conclusion: Medical therapy of varicocele with nanomicelle curcumin supplement could improve quality of semen parameters. However, further investigation is suggested in this regard.

Keywords: DNA Fragmentation; Nanomicelle curcumin ; Sperm function; Varicocele.

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A rapid nucleic acid-based amplification method for the specific identification of Klebsiella aerogenes (Research Paper)

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Introduction: Accurate identification of pathogenic bacteria is crucial for efficient therapy prescription. Culturing, biochemical tests, and molecular detection are among the common methods for the detection of bacteria in clinical labs. Nowadays, molecular diagnosis methods are becoming more prevalent. These methods are both sensitive and fast, making them extremely valuable in identifying different pathogens. Detecting bacteria at the molecular level can be achieved by amplifying the targeted sequences in the genome. Currently, isothermal amplification is gaining popularity, these techniques are better than PCR because they are faster and can be done in under an hour. This method operates at a constant temperature and does not require a thermocycler. It also uses enzymes that do not need temperature cycles. The primary objective of this research was to introduce a novel technique for the rapid and accurate detection of pathogenic bacteria at a constant temperature. In that regard, A novel isothermal amplification technique has been developed to detect Klebsiella aerogenes.

Methods: Two specific primers were designed to target a specific region in the whole genome of K. aerogenes and their specificity was checked using the Primer-BLAST tool in NCBI. Also, the bacterial samples were cultured and twelve different bacterial species including Citrobacter freundii, Serratia marcescens, Burkholderia cepacia, Yersinia enterocolitica, Pseudomonas aeruginosa, Proteus mirabilis, Morganella morganii, Enterococcus faecalis, Acinetobacter baumannii, Shigella boydii, Klebsiella pneumoniae, Salmonella typhi were utilized for specificity analysis. One colony from each species of cultured bacteria was selected to extract their genome. Nucleic acid contents were extracted using boiling and measured for equal standard concentration. The amplification reaction was set up to amplify the targeted region and detect K. aerogenes. To improve accuracy both betaine and Recombinase protein were used together with ATP. This method can be carried out at a consistent temperature in a heater block without any initial heating.

Results: The absorption of the extracted genomes was measured and no contamination was detected in the samples. Specific primers were designed based on the reaction temperature. Based on the results of the Primer-Blast Tool, the designed primer sequences were specific to the target bacterium, ensuring accurate identification. The forward and reverse primers were 31 and 32 bp, respectively and the targeted amplicon was 239 bp. The results of the amplification method showed that the entire process could be completed almost instantly in 20 minutes. The developed method successfully differentiated all tested bacteria with 100% specificity based on differentiation and color contrast between positive and negative samples.

Conclusion: In conclusion, the speed and accuracy of the method make it an appropriate choice for rapid detection tests, especially point-of-care testing and diagnostic kits. This approach significantly accelerates the treatment process and can even prevent pandemics in some cases by facilitating swift diagnoses.

Keywords: Klebsiella aerogenes, Isothermal Amplification, Rapid Diagnosis, Molecular detection

A review of ganarene and respiratory skin burns (Review)

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Introduction: Gangre is clinical condition of ischemic and necrotic tissues. The three main types of gangrene are wet gangrene, dry gangrene, and gas gangrene.The cause of gangrene maybe a bacterium called clostridium perfringe And for gas gangrene is the cause of clostridium septicum,clostridium sordellii . The spread of gangrene around the world shows that this disease is increasing in America, Turkey, and Germany. Fortunately, gangrene can be treated and with timely and quick diagnosis, the death of these people can be prevented. the pathogenesis of gas gangrene. Although several theories have been proposed to explain the pathologies, it is the general consensus that the local and systemic manifestations of gas gangrene are, in fact, related to the elaboration of potent extracellular protein toxins.

Methods: The classic features of gas gangrene caused by Clostridium perfringens type A can be attributed to the action of potent extracellular bacterial toxins on host cell function. Both α- and θ-toxins contribute to the progression of vascular injury and tissue destruction through their ability to prime leukocyte functional activity and to stimulate soluble and cell-associated proadhesive molecule expression in both leukocytes and endothelial cells. The chapter describes one physiological mechanism—that is, direct inhibition of myocardial contractility, whereby phospholipase C mediates cardiovascular collapse. Thus, therapeutic strategies directed against bacterial toxin activity in vivo, such as neutralization of toxins with specific antibodies or inhibition of toxin synthesis with antibiotics, are valuable adjuncts to traditional antimicrobial regimens.

Results: The pathogenesis of gangrene following intra-arterial injection of drugs is unclear. Clinical reports and this experiment suggest that it only follows injection of highly membrane-soluble drugs. Early swelling and disruption of capillary endothelial cells were demonstrated after intra-arterial injection of diazepam and thiopentone

Conclusion: We believe that a theory of pathogenesis based on this finding is consistent not only with our experimental findings, but with known in vitro

effects of membrane soluble drugs on cell membranes and the clinical features following intra-arterial injections in both human subjects and in animals.

Keywords: gas gangrene. closridium perfringe. pathologies

A review of the application of zinc oxide nanoparticles and their toxicity (Review)

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Introduction: One of the characteristics of nanomaterials is that in one or more of their small dimensions, the movement of electrons is very limited and causes electrons to scatter and collide with network ions, photons, and impurities, which leads to huge changes in the properties of materials. In the past few years, the use of high-tech nanomaterials in the field of medicine has become increasingly common; among all types of nanoparticles, metal nanoparticles have unique characteristics that make them superior to others, and one of these widely used nanoparticles is zinc oxide nanoparticles. According to numerous researches, zinc oxide nanoparticles have been widely used in the advancement and improvement of medical science in the treatment and prevention discussion, and for this reason, they have been given attention. For this reason, in this research, we examined and categorized the recent applications of zinc oxide nanoparticles in medical science, and of course, we also pointed out the important challenge of its possible toxicity.

Methods: All the materials obtained from the application of zinc oxide nanoparticles were searched in the Google Scholar database and key phrases such as "the use of zinc oxide nanoparticles in medical science", "the effect of zinc oxide nanoparticles in different organs of the body", "the role of zinc oxide nanoparticles in the treatment of diseases such as Cancer, diabetes and skin diseases" and keywords such as "nanoparticles" and "zinc oxide nanoparticles" were searched, but we limited the search to the last 4 years, that is, we reviewed the articles from 2019 to 2023. And we found a series of review and research articles in the period of time and finally 25 related articles categorized each of them based on keywords such as treatment, side effects, toxicity and type of target organ, in terms of different applications in medical science, and finally formed different parts of the article.

Results: Anti-cancer: They show cytotoxic effects in cancer cells and selectively make only these cells undergo apoptosis. Anti-inflammatory: reduce inflammatory cytokines. Bamboo salt contains zinc and is used to treat inflammation. Skin care and wound healing: One of the important types of zinc paste bandages contains zinc oxide nanoparticles, which are used for skin

care and leg wound treatment. Treatment of diabetes: After examining mice with type 2 diabetes, it was found that zinc oxide nanoparticles were responsible for increasing insulin levels and reducing glucose levels. Toxicity: nanoparticles can generally attack the surrounding cells and accumulate inside the blood vessels, or cause more damage to them by migrating to distant tissues or organs; Toxicity effect on brain tissue: According to the tests conducted, zinc oxide nanoparticles may have a harmful role in brain development, and on the other hand, other tests identified its protective role on the brain. Toxic effect on liver tissue: Experiments on rats showed that zinc oxide nanoparticles have a toxic pathological effect on liver function and reduce liver enzyme levels. Effects of toxicity on reproduction: it causes fertility problems through different pathways, including changing the gene expression of proteins involved in the biogenesis and function of mitochondria. Toxic effects on thyroid tissue and lysosomes: their toxic effects on thyroid gland function or the secretion of thyroid stimulating hormone may cause a decrease in the secretion of these hormones. Also, a sudden increase in the level of free zinc may damage lysosomes. It is important to note that pathological changes caused by zinc oxide nanoparticles mainly depend on their size and dose.

Conclusion: According to the studies, it was found that zinc oxide nanoparticles are widely used in medical science and are used as a safe candidate for targeted treatment. But on the other hand, it should be noted that zinc oxide nanoparticles can indirectly affect humans and the environment through contact or consumption of water, plants and animals (which previously received these nanoparticles), or directly through skin contact and inhalation. As a result, it is suggested that in the future, in addition to discovering and investigating the useful applications of zinc nanoparticles in medical science, their side effects and toxicity in different organs should also be investigated in order to reach a scientific balance between application and risk.

Keywords: Nanoparticles/zinc oxide nanoparticles/nanotechnology/medical science

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A review of the effect of massage on reducing labor pain from 2018 to 2023 (Review)

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Introduction: Childbirth is one of the most important events in a woman's life, and the pain of childbirth is the most severe pain they have ever experienced. Most of the non-pharmacological pain control techniques are non-invasive and do not threaten the health of the mother or the baby.

Methods: To identify studies aimed at the effect of massage on reducing labor pain, this systematic review was conducted in PubMed, Science Direct, and Google Scholar databases based on the keywords pain relief, labor pain, relaxing, and massage between 2018 and 2023. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed, the full text of the articles was searched, and the articles related to the topic were included in the study.

Results: According to the studies, massage is the oldest method of tactile stimulation used to relieve labor pain. However, the complete elimination of pain does not necessarily mean a more satisfying labor experience for women. Massage relaxes and reduces labor pain, relieves muscle spasms, and increases physical activity, as well as providing general relief during labor. Non-pharmacological interventions such as massage are effective labor pain management techniques because they reduce pain perception, anxiety, and stress levels, as well as the need for medication, and increase women's satisfaction with childbirth

Conclusion: Pain relief during childbirth is one of the essential aspects of midwifery care. Non-pharmacological methods do not necessarily reduce labor pain or facilitate vaginal delivery, but they can enable women to actively work with their physiological responses. Massage may help women cope with labor pain and give them a better birth experience; however, the quality of the evidence is generally low or very low

Keywords: massage, labor pain, pain relief

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A review of the effect of yoga and meditation techniques on vaginismus (Review)

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Introduction: Vaginismus is a common issue in midwifery that greatly affects women's health and sexual satisfaction. Despite being recognized as a significant problem, there is a lack of comprehensive and up-to-date information regarding effective techniques to address it. Consequently, this study was conducted to examine the impact of yoga and meditation techniques on vaginismus.

Methods: The present study is a narrative review that aimed to compile information on the topic. To gather relevant articles, the researchers conducted a computer search using databases such as Google Scholar, PubMed, ScienceDirect, Magi Ran, and Sid. To conduct the search, keywords such as vaginismus, yoga, and meditation were used. Initially, 20 articles were identified, their abstracts were examined, and the articles that did not address the research question were excluded. Subsequently, the full texts of the remaining articles were studied, and the data of 13 articles were used to develop this review article.

Results: The findings of the present research led to the classification of results into three general dimensions. The physical dimension: Yoga physical techniques have an impact on both the body and mind, aiding in the improvement of vaginismus by strengthening the control of perineal muscles. The psychological dimension: Through the practice of meditation in yoga and being mindful of emotions while focusing on breathing, individuals with vaginismus can reduce their anxiety and achieve a significant enhancement in their sexual satisfaction. The biological dimension: These techniques influence the level of gamma-aminobutyric acid (GABA) in the brain and stimulate the parasympathetic system, leading to increased relaxation and a potential reduction in symptoms such as vaginal tightness and pain.

Conclusion: The findings of this study can be disseminated to experts and healthcare professionals, enabling them to educate women about the role of

yoga and meditation in improving vaginismus. Thus, women can incorporate these techniques into their daily routines and life plans, potentially benefiting from their positive effects.

Keywords: vaginismus, yoga, meditation

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A review of the impact of gynecologic cancers on women's sexual quality of life (Review)

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Introduction: Women's sexual quality of life is one of the key issues in the field of sexual health and fertility which can be influenced by various diseases. Gynecologic cancers can negatively influence the sexual function of women. Given the fact that a limited number of studies have been conducted on these women's sexual quality of life, this study was conducted to investigate the impact of gynecologic cancers on these women's sexual quality of life.

Methods: For writing this narrative review, the researchers conducted a search in databases, including Google Scholar, Pub med, Science Direct, ProQuest, Magi ran, and Sid through using keywords such as cancer, gynecology, sexual quality of life, and women. Initially, 32 articles were found whose abstracts were studied and, then, the articles that did not answer the research question were removed. Then, the full texts of the related articles were studied and, finally, the complete data of 14 articles were used to write this review article.

Results: Based on the findings of the study, the materials were classified into the following three general dimensions. Physical effects: For women who experience gynecologic cancers, the physical consequences of cancer such as body image disturbances, hair loss, and removal of female genitals can have negative effects on their sexual function. Psychological effects: Many women with gynecologic cancers suffer from emotional distress such as feeling less feminine and less attractive, as well as psychological consequences such as death anxiety and fear of recurrence, which can affect their sexual quality of life. Therapeutic effects: Cancer treatments such as surgery and chemotherapy can lead to problems in women's sexual quality of life, such as decreased sexual desire, lack of pleasure and excitement, orgasmic dysfunction, pain, and decreased frequency of sexual intercourse.

Conclusion: The results of this study can be used by the Ministry of Health and the health officials who are in charge of women with gynecologic cancer

to develop educational and counseling programs as complementary treatment methods along with cancer treatment in the treatment protocol of these patients in order to improve their sexual quality of life.

Keywords: Cancer, gynecologic, sexual quality of life, women

A Review of the Impact of Microbial Contamination in Non-Sterile Oral Drugs (Review)

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Introduction: Microbial contamination in non-sterile oral drugs poses a significant risk to public health. This comprehensive review aims to assess the impact of microbial pathogens in non-sterile oral drugs and provide an overview of the associated risks and challenges.

Methods: This review assesses the impacts of microbial contamination on non-sterile oral drugs and the potential consequences for patients. It examines references related to microbial specification, types of pathogens, and their sources. It also investigates the infections caused by these pathogens and the prevalence of microbial contamination. Furthermore, the review explores current methods for detecting, identifying, and establishing the standard range of dangerous microbial pathogens in non-sterile oral drugs.

Results: Microbial contamination in drugs poses an infectious risk and can alter the chemical, physical, and organoleptic properties of the drugs and the contents of active ingredients. Additionally, microorganisms can convert drugs into toxic products. Regardless of the dosage form and route of administration, non-sterile oral drugs must adhere to microbiological purity criteria outlined in the appropriate editions of the EP and USP. This includes checking for specific pathogens and monitoring the Total Aerobic Microbial Count (TAMC) and Total Mold and Yeast Count (TMYC). Microbial contamination can occur through various means, such as the environment, high humidity levels, and uncontrolled air quality. It can also arise from natural raw materials, contaminated water, poor personal hygiene practices, open wounds, coughing and sneezing, dirty hands, feces, and soiled clothing.

Conclusion: This review emphasizes the need to continuously assess microbial pathogens in non-sterile oral drugs to protect public health and improve patient outcomes. Collaboration between regulatory authorities, pharmaceutical companies, and healthcare providers is essential in addressing this issue. Adhering to Good Manufacturing Practice (GMP) guidelines and implementing effective quality control measures throughout

production are crucial for reducing the risk of microbial contamination in pharmaceutical products.

Keywords: microbial contamination, non-sterile oral drugs, pathogens, prevalence, public health.

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A review of The role of stress in cancer (Review)

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Introduction: There is evidence that hormones related to stress and anxiety and environmental neurotransmitters can cause proliferation, survival, angiogenesis, and tumorigenesis. Sometimes it strengthens them and disrupts the immune response. The mentioned changes cause a change in the endocrine system's signaling pathways, disturb the body's balance, and stimulate the immune response. Stress stimulates the hypothalamus-pituitary axis and the parasympathetic system, resulting in the abnormal secretion of hormones that activate signaling pathways and increase downstream oncogene expression. It increases active tumorigenesis, angiogenesis, and metastasis.

Methods: In this review study, a search was made in electronic and scientific databases PubMed, Google Scholar, and Scopus, and valid articles related to the subject were searched using the keywords stress and cancer.

Results: Stress definitely plays a role in the spread of cancer by disrupting the immune system. Also, controlling stress and strengthening the body's immune system can play an important role in preventing and treating diseases such as cancer.

Conclusion: Considering that the role of stress is important in the development of various diseases, including cancer, in this sense, studying and researching in this field is a key step in the treatment and prevention of cancer and other related diseases.

Keywords: Stress, Cancer, Immune system

A Review on NSAIDs and its effect on Cardiovascular Disorders (Review)

Negar taghizadeh ,[1] Mohammad daily ,[2,*]

1.
2.

Introduction: Drugs that have analgesic and antipyretic properties are known as nonsteroidal anti-inflammatory drugs (NSAIDs) in general. It is commonly acknowledged that there is a chance of blood pressure increase and heart failure. The known information on the Cardiovascular risk of NSAIDs, their potential therapeutic effect, and the putative processes behind the elevated incidence of cardiovascular events seen with NSAID treatment are summarised in the article that follows.

Methods: Review

Results: According to a research by Heerdink et al. (1998), when NSAIDs were given to patients on diuretic treatment, the risk of hospitalisation for heart failure was increased by 1.8 (95% CI= 1.4-2.4). The lack of a substantial difference between individual NSAIDs observed by the authors supports a class effect within the initial few days of starting therapy, the risk of heart failure subsequently dropped to reach placebo levels after a month. Page and Henry (2000) also looked at the possibility of heart failure hospitalisation when using NSAIDs. When compared to non-users, NSAID users had a relative risk. The RR was notably greater in individuals with prior existing cardiovascular disease (10.5). The authors speculate that up to 19% of instances of newly diagnosed congestive heart failure may be related to the use of NSAIDs. In their cohort trial, Mamdani, et al. (2004) examined the likelihood that patients using coxibs, non-selective NSAIDs, and controls would need medical treatment for heart failure. Patients using rofecoxib had the highest risk (RR = 1.8, 95% CI= 1.5-2.2). Users of non-selective drugs had a relative risk of 1.4 (95% CI= 1.0-1.9). Since patients with CHF are less likely to receive an NSAID prescription than patients with other types of cardiovascular disease, new data suggests that the perception of the risk of CHF exacerbation caused by NSAIDs is higher in the medical community than the perception of the risk of other cardiovascular adverse effects (Castelli et al., 2017). Reduced glomerular filtration and salt and water excretion may result from inhibition of prostanoid synthesis in the kidney. As a result, NSAIDs raise the possibility of hypervolemia and aggravating heart failure. Patients who have compromised renal or cardiac function are at higher OF

congestive heart failure (CHF), particularly if it is being treated with diuretics (Page and Henry, 2000).

Conclusion: The current state of the data indicates that all NSAIDs are linked to a higher risk of unfavourable cardiovascular events. There are a number of variables at play, including COX-2 selectivity, dose, half-life, effects on blood pressure, and aspirin interactions. The balance of the evidence continues to favour naproxen as the safest NSAID from a cardiovascular perspective, with both the caveat that it could pose a greater risk for an upper GI bleed than other tNSAIDs. The shortcomings of these two trials only serve to cast doubt on any conclusions made regarding the comparative safety of the NSAID agents studied, leaving the question of differential cardiovascular risk unanswered. When using NSAIDs, patients with congestive heart failure run the danger of the condition decompensating. Patients who use diuretics are most at risk, particularly in the first weeks after receiving NSAID therapy. In conclusion, it should be emphasised that older individuals who often have arterial hypertension, CHF, and coronary artery disease are typical candidates for long-term prescription of NSAIDs. The risk of serious cardiovascular consequences is consequently very often increased in chronic NSAID users. To enhance patient safety while receiving NSAID medication, adequate monitoring for adverse impact signs and symptoms and appropriate patient education are needed. Only the lowest effective dosage should be used during NSAID therapy, and the duration should be kept as short as the clinical circumstances permits.

Keywords: Keywords: NSAID, Cardiovascular Disorders

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A review on Preimplantation Genetic Testing (PGT) for chromosomal abnormalities diagnosis. (Review)

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Introduction: It's important to recognize how chromosomal abnormalities impact human reproduction. Researches show that natural fertility in humans follows an inverse U-curve during maternal reproductive years. This indicates that embryonic chromosomal abnormalities caused by meiotic errors during oocyte formation are the primary reason for reduced potential at both ends of the curve. This phenomenon is unique to humans. On average, even at the peak of a woman's fertility, chromosomal abnormalities affect around 20% of oocytes. It has been observed that around 50% of preimplantation human embryos possess chromosomal abnormalities. This is due to some level of error-proneness behavior during chromosome segregation in gametogenesis, which is actually beneficial for our species. It is important to understand that embryonic chromosomal abnormalities are not an anomaly but rather a planned and fundamental aspect of the natural reproduction process in humans. Chromosomal abnormalities, including aneuploidy (which is the most common genetic abnormality found in humans. Their high incidence in embryos is the main cause of failed implantation, pregnancy loss, and congenital birth defects. Typical examples are monosomy or trisomy, respectively resulting in 45 or 47 chromosomes.), chromosomal mosaicism (which occurs when cells have different chromosomal constitutions. The relevant type for PGT-A is a mix of euploid and aneuploid cells.), segmental abnormalities (refer to changes that occur in specific sections of chromosomes, and these changes often result in regional losses or gains.), structural rearrangements (abnormalities that alter the natural order of chromosomal segments but do not affect copy numbers. Include Balanced translocations, robertsonian translocations, insertions, and inversions.) Preimplantation Genetic Testing (PGT) helps detect chromosomal abnormalities and conditions that affect embryo health and viability.

Methods: In this review study, we analyzed articles related to modern fertility from 2015 to 2023, obtained from the PubMed and Google Scholar databases.using keywords such as preimplantation genetic testing; PGT; preimplantation genetic diagnosis; PGD; genetic screening; aneuploidy; genetic testing methods; comprehensive chromosome screening; next-generation sequencing; next-generation screening; NGS; comparative

genomic hybridization; CGH; array comparative genomic hybridization; aCGH; single nucleotide polymorphism; SNP polymerase chain reaction PCR; quantitative polymerase chain reaction; quantitative real-time polymerase chain reaction; etc.

Results: In the past, PGT mainly relied on the Fluorescent In Situ Hybridization (FISH) technique. But today, modern methods such as array, Next-generation sequencing (NGS), SNP, array CGH, and quantitative PCR (qPCR) are now more commonly used to examine all 24 chromosomes. Among these methods, NGS is generally considered the most suitable for PGT-A, as it can diagnose mosaicism effectively. While Array CGH has many advantages, it does have a limitation in detecting polyploidy. It is particularly useful in detecting subchromosomal disorders (segmental aneuploidy), but it's important to consider the size of such disorders, especially if there is a history of that disorder in the family tree, especially in the parents. After using the FISH technique to examine the first polar body resulting from meiosis I, it was discovered that up to 24% of cases showed aneuploidy. This percentage was influenced by the number and type of chromosomes examined, as well as the clinic conducting the examination. However, an array CGH studies that examined all chromosomes reported an even higher percentage of aneuploidy. As for meiosis II, examinations of the second polar body showed approximately 37% aneuploidy with FISH and 46% with CGH. Part of the differences between FISH results and 24-chromosome methods is due to the limitation of the number of chromosomes that can be examined in the FISH method. What should be noted in the meantime is that meiotic aneuploidies are expected to result in embryos with the same aneuploidy in all cells. Women over 35 years old who have aneuploidy in their eggs before implantation may be directly affected by their age. However, examining the polar body of the egg is not a reliable method for predicting the fetus's genetic status. Reports on aneuploidy during the third embryonic day vary depending on the technique used. Using the FISH technique, 25 to 83% of embryos are reported to be abnormal at this stage. This stage of development appears to have the highest incidence of division disorders. Clinical studies on PGT based on blastocyst biopsy show nearly 60% aneuploidy, with much of it being mosaicism. Examining aneuploidy during the blastocyst stage has an advantage since several trophoectoderm cells are biopsied, which increases the chances of detecting mosaicism and reduces the possibility of not getting an answer.

Conclusion: Although PGD is a widely accepted procedure, there is still ongoing debate regarding the acceptance of PGT-A. This will depend on advancements in our understanding of human embryo development and the

success of biopsy strategies when combined with genetic analysis. It appears that there is a consensus that mosaicism is less problematic when performing trophoectoderm biopsy compared to embryo biopsy at the cleavage stage.

Keywords: chromosomal abnormalities, Preimplantation Genetic Testing, PGT.

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A review on the effect of qnrVC gene on the virulence and antibiotic resistance of Pseudomonas aeruginosa bacteria (Review)

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Introduction: Pseudomonas is a genus of Gram-negative pathogenic bacteria that leads to infectious diseases in both plants and animals [1]. The emergence of P. aeruginosa as a major opportunistic human pathogen during the past century may be a consequence of its resistance to the antibiotics and disinfectants that eliminate other environmental bacteria [2]. Due to the extensive capabilities for regulation, survival and resistance to multiple classes of antimicrobials, P. aeruginosa strains diseases can be life-threatening and are developing worldwide as an open health risk. One of these broad capabilities is genomic resistance, and P. aeruginosa strains have broad genomes.They have a wide metabolic capacity. Specifically, they are characterized by a high capacity to deliver multiple metabolites and co-polymers, as well as to utilize different carbon sources and electron acceptors. Some diseases caused by Pseudomonas aeruginosa bacteria such as: urinary infections, respiratory tract, skin, inflammation and swelling, soft tissue infections, bacteremia (the presence of bacteria in the blood), bone and joint infections, stomach and intestinal infections and There are different types. Systemic infections, especially in patients with severe burns, cancer and AIDS patients whose immune system is suppressed [3]. The qnrVC family was first described in Vibrio cholerae in 2008. It is indirectly related with: lasB, toxA, exoS,algD, these genes are more involved in various infections like skin infections [4].

Methods: qnrVC genes have been demonstrated as a source of anti-microbial resistance and also causes infection, and this conflict infection can be of the skin type [5]. Multiple studies have been done about qnrVC genes that shows the role of this genes in multidrug-resistance Ralstonia pickettii wound infection in some patients [6].

Results: Skin is the human body's largest organ. It plays a vital role as the primary protective barrier of the body against pathogens, chemical, and mechanical stresses [1]. when this integral barrier is damaged, an ulcer or wound can form. An open wound becomes a suitable place for a wide range

of microorganisms, including Staphylococcus aureus and Pseudomonas aeruginosa. Also, this gene (qnrVC) is prevalence in foodborne and communicate with gryA and parC genes, which are commonly associated with ciprofloxacin resistance. Fourteen qnrVC variant genes that contained novel mutations were detected. In this review, we mentioned the role of qnrvC gene in antibiotic resistance and increasing the intensity of infection. For a long time, P. aeruginosa has been a stable form of life and has attracted the attention of the rational community to think about the way of life and bacterial pathogenesis. It continuously has been of specific significance due to causing tireless contaminations in CF and immunocompromised patients.

Conclusion: These days, P. aeruginosa is recognized worldwide as an open health risk due to its increasing resistance to various classes of antimicrobials. Over the past decade, extensive inquiries into reflection have focused on these developing concerns. qnrVC genes have been shown to be the source of antimicrobial resistance, but more studies are needed, and the ones mentioned are still not enough.

Keywords: Antibiotic resistance, Infection, Genes, Pseudomonas aeruginosa, qnrVC.

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A scorpion-derived alpha toxin: characterization and homology modelling (Research Paper)

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Introduction: Scorpion venom likes a treasure because of having medically important components. Venom of scorpion consists of a mixture of peptides and proteins, some of them are toxic. Ion channel modifiers are the most important of them. Some drugs have designed based on the snake and scorpion venoms. So, identification and characterization of venom compounds can be a useful path for drug discovery.

Methods: Here, analysis of transcriptome obtained from the venom gland of M. eupeus using total RNA extraction and cDNA library synthesis; revealed the presence of some toxin transcripts. Blasting the transcriptome against proteins databases, including NCBI and Uniprot was done to find alpha toxin(s). Physico-chemical properties one determined alpha toxin was calculated using bioinformatics software. Finally, Three-dimensional structure of this protein was determined by means of homology modelling.

Results: According to the blast we found a sodium channel blocker, alpha toxin in the venom of M. eupeus, named meuNaTx-2 and deposited in the Gene bank. The mature peptide of meuNaTx-2 has 66 AA. A molecular weight of, 7482g/MOL and a theoretical pI of 8.12 were estimated for it. Secondary structure analysis determined a Toxin-3 superfamily domain in the structure of this protein. meuNaTx-2 has eight cysteine residues, which forms four disulphide bridges contributed in a conserved cysteine-stabilized alpha/beta domain. The three-dimensional structure of meuNaTx-2 consists of one alpha-helix and two beta-sheets, each of them contains two beta-strands.

Conclusion: Analysis of transcriptome of M. eupeus venom glands identified an alpha toxin which potentially modify sodium channels. Characterization and structure of this protein showed that it can be a great candidate for more research. Herein reported information about this protein can lead us to further investigation about function or probably using in drug design.

Keywords: Sodium channel blockers, Scorpion venom, Alpha toxin

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A Study of Cariprazine's effect on tau microtubule-associated protein (2MZ7) by molecular docking method (Research Paper)

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Introduction: Tau is considered one of the most significant proteins involved in binding and stabilizing microtubules, constituting over 80% of neuronal microtubule- associated proteins.1 As a result, tau's mutation or hyperphosphorylation is highly involved in the development of different progressive neurodegenerative disorders like Alzheimer's disease (Figure 1).2 As a new dopamine D2 receptor partial agonist, Cariprazine, has been investigated in a variety of psychiatric disorders, including schizophrenia, bipolar disorders, and major depressive disorder.3,4 Our purpose of this study was to determine whether this antipsychotic Drug can bind to the tau protein receptor as a ligand.

Methods: Through the docking strategy, which is an analytical descriptive technique, we first downloaded the 3D structure (Pdb) of the tau protein (267-312 nucleotides) from the UniProt site (Figure 2). Then, through the Chimera software (Version.1.17.1), we made the required adjustments such as removing solvents, evacuating water molecules, adding flux, etc. In the following step, we downloaded the 3D structure of Cariprazine (427.4 g/mol) from the PubChem site (Figure 3). In addition, we selected the appropriate grade box by using a molecular spatial analysis, performed by Deepsite (Vina data/ X=16:2092, Y= -6.1601, Z= -20.9144). Drug and protein were placed as ligand and receptor in PyRx software (Version.0.8). Both Data were selected separately and the docking process started. The Data output was checked as an Excel file.

Results: According to the docking process, the results were as follows.
(Table 1.) LIGAND BINDING AFFINITY RMSD/UB RMSD/LB
FINALPRP_11154555_UFF_E=451.93 -5.4 0 0
FINALPRP_11154555_UFF_E=451.93 -5.3 3.187 2.375
FINALPRP_11154555_UFF_E=451.93 -5.2 9.298 5.019
FINALPRP_11154555_UFF_E=451.93 -5.2 4.504 2.842
FINALPRP_11154555_UFF_E=451.93 -5.2 9.085 4.521
FINALPRP_11154555_UFF_E=451.93 -5.2 5.247 2.852
FINALPRP_11154555_UFF_E=451.93 -5.1 1.989 1.401
FINALPRP_11154555_UFF_E=451.93 -5 12.391 8.372

FINALPRP_11154555_UFF_E=451.93 -5 12.48 7.937 Table 1. Vina Wizzard's Data indicating Cariprazine-Tau's binding affinity and rmsd

Conclusion: Tau is one of the key proteins in Alzheimer's disease, on which many studies are conducted. As claimed by Docking results, we found that there is a probability of binding Cariprazine to the tau protein, therefore the clinical trial period of this drug can begin in the field of Alzheimer's disease.

Keywords: Keywords: tau microtubule-associated protein, Cariprazine, Docking method, Alzheimer's disease

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Accuracy of Focused Assessment with Sonography in Trauma (FAST) Compared to CT Scan in Patients with Blunt Abdominal Trauma (Research Paper)

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Introduction: Objective: Focused assessment with sonography in trauma (FAST) is a very valuable part of the initial examination in emergency care. the aim of this study is to define the recent role of FAST and CT scan of the abdomen in the diagnosis of blunt abdominal trauma.

Methods: Method: A cross-sectional study on 150 blunt abdominal trauma patients who were admitted to the emergency department of Khatam Zahedan Hospital in 2021. The findings of FAST and CT scan were compared after extracting from the patient's records. In comparison to CT Scan as a reference, the sensitivity, specificity, PPV and NPV of FAST were evaluated.

Results: Findings: The patients included 109 men and 41 women with an average age of 35.7 ± 25.8 years, the youngest was 19 years old and the oldest was 70 years old. The most injuries were due to accidents (40 cases), falls (50 cases) and impact (60 cases). The condition of the patients was such that about 97% of the patients had triage level 2. The sensitivity was 75%, the specificity was 98.6%, the positive predictive value was 60%, and the negative predictive value was 99.3%.

Conclusion: Conclusion: FAST is a high diagnostic value in the screening of patients with blunt abdominal trauma. FAST is a reliable tool for examining trauma patients and due to the constant presence of emergency medicine specialists at the patient's bedside in the early moments, it plays a significant role in improving the treatment protocol of trauma patients.

Keywords: Keywords: blunt abdominal trauma, FAST, CT Scan, sensitivity, specificity, PPV, NPV.

Acrylamide as a Possible Factor Responsible for Inflammation in the Nervous System (Review)

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Introduction: Acrylamide (ACR) is a chemical compound that exhibits neurotoxic and genotoxic effects.It causes neurological symptoms such as tremors, general weakness, numbness, tingling in the limbs or ataxia. Numerous scientific studies show the effect of ACR on nerve endings and its close connection with the cholinergic system. The cholinergic system is part of the autonomic nervous system that regulates higher cortical functions related to memory, learning, concentration and attention. Within the cholinergic system, there are cholinergic neurons, anatomical cholinergic structures, the neurotransmitter acetylcholine (ACh) and cholinergic receptors. Acrylamide (ACR) is an organic chemical compound with the chemical formula C3H5NO. It is composed of carbon (50.69%), hydrogen (7.09%), nitrogen (19.71%) and oxygen (22.51%) atoms. At room temperature, it is an odorless, crystalline solid with a molecular weight of 71.08, a melting point of 84.5 _C and a density of 1.122 g/cm3 at 30 _C. Due to its relatively low volatility, its boiling point is 192.6 _C at a pressure of 1 atm (101.3 kPa). Due to the presence of functional groups, this compound is polar and very soluble both in water and in other polar solvents such as methanol or ethanol. However, it is insoluble in benzene and heptane. The aim of the study was to review the current state of knowledge of the influence of acrylamide on the cholinergic system and its possible effect on inflammatory processes.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Some scientific reports suggest a negative effect of ACR on the cholinergic system and inflammatory reactions within the body. The cholinergic anti-inflammatory pathway (CAP) is a neuroimmunomodulatory pathway that is located in the blood and mucous membranes. The role of CAP is to stop the inflammatory response at the appropriate moment. It prevents the synthesis and release of pro-inflammatory cytokines and ultimately regulates the local and systemic immune response. The cellular molecular mechanism for inhibiting cytokine synthesis is attributed to acetylcholine (ACh), the major vagal neurotransmitter, and the 7 nicotinic receptors (7nAChR) subunit is a key receptor for the cholinergic anti-inflammatory

pathway. The combination of ACh with 7nAChR results in inhibition of the synthesis and release of pro-inflammatory cytokines. The blood AChE is able to terminate the stimulation of the cholinergic anti-inflammatory pathway due to splitting ACh. Accordingly, cytokine production is essential for pathogen protection and tissue repair, but over-release of cytokines can lead to systemic inflammation, organ failure, and death. Inflammatory responses are precisely regulated to effectively protect against harmful stimuli. The central nervous system dynamically interacts with the immune system, modulating inflammation through the humoral and nervous pathways. The stress-induced rise in acetylcholine (ACh) levels acts to ease the inflammatory response and restore homeostasis. This signaling process ends when ACh is hydrolyzed by acetylcholinesterase (AChE). There are many scientific reports indicating the harmful effects of ACR on AChE. Most of them indicate that ACR reduces the concentration and activity of AChE. Due to the neurotoxic effect of acrylamide, which is related to the disturbance of the secretion of neurotransmitters, and its influence on the disturbance of acetylcholinesterase activity, it can be concluded that it disturbs the normal inflammatory response.

Conclusion: Studies on the harmful effects of acrylamide and its metabolites indicate three possible types of toxicity: neurotoxicity, genotoxicity, and carcinogenicity. So far, only the neurotoxic effect of acrylamide on the human body has been undoubtedly proven. The studies conducted so far indicate, first of all, the reduction of acetylcholinesterase activity. The genotoxic activity of acrylamide is mainly manifested after its metabolic conversion to the epoxide derivative glycidamide. The carcinogenic effect of acrylamide has been demonstrated in animal studies. For humans, exposure to acrylamide is assessed as evidence that acrylamide ingested with the diet can initiate the formation of cancer in humans and induce an inflammatory response.

Keywords: Acrylamide, Inflammation, Nervous System

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Adaptive laboratory evolution technology for the production of medicinal docosahexaenoic acid from Aurantochytrium strain (Research Paper)

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Introduction: Therostochytrids are aerobic and marine heterotrophic microorganisms that include genera such as Therostochytrium, Schizochytrium, Japonochytrium, and Aurantochytrium. Aurantochytrium is a single-cell marine oleaginous microorganism that is able to accumulate a large amount of omega-3 fatty acids and docosahexaenoic acid. These oils are a sustainable substitute for fish oil. Docosahexaenoic acid fatty acid prevents the occurrence of cardiovascular diseases and contributes to the proper functioning of the brain and eye health. Chronic inflammation is a risk factor for cancer, and the consumption of omega-3 fats such as docosahexaenoic acid, which has anti-inflammatory effects, reduces the risk of developing cancer, including colon, pancreatic, breast, and prostate cancer. Also, docosahexaenoic acid can have the benefits of chemotherapy. It improves treatment and cellular studies show that it may even inhibit the growth of cancer cells.

Methods: Optimizing the culture medium of Aurantochytrium strain was done with laboratory adaptive evolution technology and then the amount of cell dry weight, oil and docosahexaenoic acid was calculated. By using this technology, the cells are adapted to the selected conditions in the culture environment and during successive generations, and their growth and production are increased. The parameters considered in carrying out laboratory adaptive evolution technology include the effective Faulknor of glucose concentration, factor sensitivity test, determining the concentration or amount of selective pressure, selecting the final level of selective pressure or two higher levels, and finding the species adapted to stress conditions. In the optimization of the culture medium of Aurantochytrium strain, glucose was measured in six concentrations of 1%, 2%, 3%, 5%, 7%, 10% in the medium containing artificial seawater, yeast extract, peptone water.

Results: By calculating the cell dry weight of the concentration The optimal glucose used was %10.

Conclusion: The results showed that during ten consecutive generations, the amount of biomass and oil in ALE 10 strain increased compared to the parent strain.

Keywords: docosahexaenoic acid, Aurantochytrium , Adaptive laboratory evolution, Glucose

Advances in Wound Healing and Skin Tissue Regeneration (Review)

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Introduction: The skin is the largest organ in the body and its main function is to protect against environmental influences through the immune response. Skin ulcers are a pathological condition caused by disease or physical/chemical damage, and they can be classified as acute or chronic wounds depending on their origin and duration of recovery. Acute wounds are caused by traumatic injuries or surgical procedures, while chronic wounds are often associated with infections, vascular disease, diabetes, and cancer. The healing process of a wound depends on its size, depth, and damage to the layers of the skin. Factors such as nutritional or immunological weakness, age, chronic stress, and other co-morbidities can also affect the recovery process. Treating chronic wounds has become a significant financial burden, with millions of patients affected in the United States alone. The annual cost of treating chronic wounds exceeds $25 billion and is expected to rise due to increasing healthcare costs, an aging population, and the growing incidence of diabetes and obesity worldwide. Projected medical costs for all wounds range from $28.1 billion to $96.8 billion, including infection management and wound repair costs. The process of skin wound healing can be categorized into three distinct biological stages: inflammation, proliferation, repair, and regeneration. Throughout the healing process of injuries, a variety of mechanisms are involved, such as coagulation, accumulation, inflammation, synthesis and deposition of matrix, angiogenesis, fibroplasia, epithelialization, contraction, and regeneration . The normal progression of wound healing can be further divided into four phases: the coagulation phase, the inflammatory phase, the proliferative/tissue formation phase of granulation, and the regeneration phase.

Methods: To discover the latest developments in the field of wound healing and skin tissue regeneration, we conducted a thorough search using the

PubMed and Google Scholar databases. We used specific keywords such as wound healing, regenerative medicine, skin, tissue engineering, cell therapy, fibroblast, platelet-rich plasma, and gene therapy. This comprehensive search covered the period from 2000 to 2023 and provided the possibility of a comprehensive review of the subject.

Results: Significant progress has been made in the field of wound management and wound healing. These advances include improvements in clinical techniques for treating wounds, such as skin grafts, skin substitutes, biological wound dressings, and topical antimicrobial agents, as well as the administration of systemic antibiotics. In addition, pharmacological approaches including corticosteroids, TGFβ modulators, and botulinum toxin A are used for wound management. Other treatment methods include surgical procedures such as fat grafting and scar modification through laser therapy. Today, in order to repair all types of burn wounds, diabetic wounds, deep wounds and pressure wounds, extensive studies are conducted with the help of tissue engineering and regenerative medicine. Tissue engineering and Regeneration can be divided into four main categories: tissue scaffolds, growth factors, cells, and gene therapy. Fibroblasts, adipose-derived stem cells, and keratinocytes are common cells in skin wound healing. Dermal fibroblast cells play an important role in normal skin as well as wound healing after injury.

Conclusion: Cell Therapy are used in autologous and allogeneic form, by injecting into the wound, spraying and with the help of scaffold. The presence of fibroblasts is vital in the stages of wound healing and they play a key role in the deposition of extracellular matrix (ECM) components, wound contraction and regeneration of new ECM. Cells survive for a limited time, and are used as a source of growth factors and cytokines to support the function of the patient's own cells. During extensive studies, the effect of gene therapy on the healing of skin wounds has been measured.The list of genes examined in these studies is as follows: PDGF-B, SDGF-1α, VEGF-A, IL-8, TGFβ1, EGF, FGF-1 and fibromodulin.

Keywords: wound healing, skin, regenerative medicine, fibroblast.

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Advancing Chronic Lymphoblastic Leukemia Management: A Systematic Review of Preclinical Studies on Nanotechnology-Based Diagnostics and Therapeutics (Review)

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Introduction: Background: Chronic Lymphoblastic Leukemia (CLL) continues to pose challenges, in its diagnosis and treatment. However nanotechnology holds promise as a solution by enabling precise targeting and improving treatment effectiveness. This comprehensive review aims to evaluate studies that explore the use of nanotechnology for diagnosing and treating CLL.

Methods: Methods: To conduct this review we searched databases for preclinical studies that employed nanotechnological interventions in CLL diagnosis or therapy. We assessed the quality of the methods used in these studies analyzed their outcomes and extracted data.

Results: Results: Our findings from the experiments showed that TNF α have effects on different types of cancers. While some cytokines promote cell growth others exhibit effects. Moreover these cytokines demonstrate nuanced roles in tumor metastasis by influencing migration and invasion capabilities. The systematic review supported these multifaceted roles by highlighting context influences on tumor progression across malignancies.

Conclusion: CONCLUSION: Consequently, this systematic review highlights how nanotechnology is expanding the landscape of tools and therapeutic options for managing CLL. Preclinical evidence suggests that nanotechnology offers opportunities to advance precision medicine and improve treatment outcomes for patients, with CLL. However further research is needed through

studies and clinical trials to validate these findings before they can be applied in world clinical settings.

Keywords: Keywords: Neoplasm, Tumor necrosis alpha, Metastasis, Proliferation, Systematic Review

affect poisoning on pregnant mother and birth outcomes: A narrative review (Review)

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Introduction: Pregnancy is a high-risk period of a mother's life because many factors can affect the mother's and fetus's health and growth, and this time needs exact evaluation. Poisoning during pregnancy is the cause of mortality and morbidity of mothers and their fetus. It was reported that 0.3% of all the poisoning in America yearly happened during pregnancy. Carefully analyzing the type of component, treatment, time, and type of exposure can lead to a general view for better intervention and decrease problems during pregnancy due to poisoning. This study aims to investigate factors and causes of poisoning during pregnancy and birth outcomes of pregnant mothers and mother health after poisoning.

Methods: This comprehensive study was conducted by searching scientific databases, including PubMed, Google Scholar, and Scopus, with "Poisoning" and "Pregnancy" keywords during the last ten years of English articles. The subject was the poisoning of pregnant women with different components and birth outcomes.

Results: This comprehensive study was conducted by searching scientific databases, including PubMed, Google Scholar, and Scopus, with "Poisoning" and "Pregnancy" keywords during the last ten years of English articles. The subject was the poisoning of pregnant women with different components and their children's birth outcomes. The result of the previous studies investigated that the most common cause of poisoning during pregnancy was medication poisoning, that the use of Benzodiazepines and painkillers in high doses was prevalent, and in the next step of poisoning with Pesticides and drugs was prevalent. Most of the poisoning happened of Self-harm intentionally and, in the 1st and second trimesters of pregnancy, suicide history was seen in some mothers. Notably, poisoning with CO was also shared and unintentional in pregnant women. CO may lead pregnancy to abortion and mother to danger of death. Oxygen therapy is indicated in CO-poisoned mothers. The pregnant mother's average age has been under 25, and pregnant with their first child. Poisoning during this period affected the children's health and growth, and children birthed with poisoning history needed to follow up to grow up normally.

Conclusion: Poisoning can affect the mother's and fetus's health. Mothers can be poisoned intentionally or unintentionally due to many factors, and it is essential to know the common reasons for dealing with referred poisoned mothers and following up with their children after birth to reduce the risk of future problems.

Keywords: Poisoning, Pregnancy, Birth outcomes

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Air pollution as a lifespan reducer (Review)

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Introduction: One of the huge global concern is air pollution. Air pollution can affect people's life in many aspects. One of the critical aspect is Mental health. Air pollution can affect mental health in several ways. Air pollution can be neurotoxic and associated with structural brain changes. Some studies provide a basis for analyzing the relationship between air pollution and mental health

Methods: Some studies show significant associated with hospitalizations for schizophrenia in female subjects living in Beijing (China) when air pollution raised. Furthermore, there is association between air pollution and higher number of visits in the psychiatric emergency unit in Sweden during warm seasons. sulfur dioxide (SO2) air concentrations were significantly associated with an increased number of psychiatry hospitalizations especially in warm season: A Chinese study investigated the effect of different air pollutants on number of daily hospital admissions for mental disorders

Results: Some air pollutants play main role in these symptoms: PM, NO2 and SO2. Increased levels of PM may have a role in aggravating symptoms of existing mental disorders. Some mental disorder that air pollution can because of them are: Schizophrenia- Bipolar disorder –Depression- Suicide- Anxiety- Other adult mental disorders (Obsessive Compulsive Disorder, Eating Disorders or Personality Disorders)- Attention deficit hyperactive disorder (ADHD)- Autism

Conclusion: There is a report that shows association between air pollution and risk of suicide, related to increments of CO and NO2, especially for males during winter period

Keywords: Public health industrial air pollution pollution. Schizophrenia ADHD

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AKAP4 gene expression and its correlation with sperm motility and morphology (Research Paper)

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Introduction: Generally, about 15% of couple's experience infertility, which the World Health Organization (WHO) defines as failure to achieve pregnancy after one year of unprotected sex between couples. Men are responsible for half of the reasons for infertility, which has a greater prevalence in developed countries and threatens the mental health of families. The main objective of the current study was to investigate the expression of A-kinase anchor protein 4 (AKAP4) as a gene that plays an essential role in sperm motility in individuals with asthenozoospermia and terato-asthenozoospermia. Alterations in AKAP4 expression and the correlation between their expression and normal sperm morphology and motility were also examined.

Methods: This study examined the semen of 25 asthenozoospermia individuals (AZ), 27 terato-asthenozoospermia (TAZ) individuals, and 29 normospermia (NZ) individuals with normal sperm as a control group. The expression levels of AKAP4 in the sperm samples were analyzed by real-time PCR.

Results: Gene expression analysis revealed a significant association between AKAP4 expression and sperm motility and morphology ($p<0.0001$). The AKAP4 expression levels in the TAZ group was 2.56-fold ($p<0.003$) lower compare to NZ group. Also, The AKAP4 expression levels in the AZ group was 2.24-fold ($p<0.004$) lower compare to NZ group.

Conclusion: changes in AKAP4 gene expression could affect sperm's normal motility and morphology.

Keywords: asthenozoospermia, infertility, AKAP4, terato-asthenozoospermia

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Alamandine Injection in the Periaqueductal Gray and Rostral Ventromedial Medulla Attenuates Allodynia Induced by Sciatic Nerve Ligation in Rats (Research Paper)

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Introduction: Alamandine, a peptide known to interact with Mas-related G protein-coupled receptor subtype D (MrgD), has been implicated in moderating inflammatory signals. MrgD receptors are abundantly found in pain transmission pathways, but the role of alamandine/MrgD in pain modulation has not been thoroughly explored.

Methods: This study aimed to investigate the effects of alamandine (in doses of 10, 40, and 100 pmol) in a rat model of allodynia induced by sciatic nerve ligation, with a specific focus on examining the involvement of MrgD receptors in key brain regions associated with pain modulation, namely the ventrolateral periaqueductal gray (vlPAG) and rostral ventromedial medulla (RVM).

Results: Microinjection of alamandine into the vlPAG at a dose of 100 pmol and into the RVM at doses of 40 and 100 pmol resulted in a significant increase in paw withdrawal threshold (PWT), indicative of a reduction in allodynia. The inhibitory effects of alamandine were found to be dose-dependent, with higher doses eliciting stronger analgesic responses. Additionally, co-administration of D-Pro7-Ang-(1-7) at 50 pmol, an MrgD receptor antagonist, effectively blocked the analgesic effects of alamandine, highlighting the critical involvement of MrgD receptors in mediating its effects. Immunofluorescence analysis confirmed the expression of MrgD receptors in the vlPAG and RVM regions. Notably, we observed an upregulation of MrgD receptor expression following the induction of allodynia, indicating a potential compensatory mechanism in response to pain. These findings underscore the significance of MrgD receptors in pain modulation and suggest their involvement in the action of alamandine.

Conclusion: The significant inhibitory effects of alamandine on allodynia, coupled with the presence and upregulation of MrgD receptors, highlight its promising therapeutic potential as a modulator of allodynia. Further investigations into the underlying mechanisms and signaling pathways involved in alamandine-induced analgesia and MrgD receptor function are warranted to comprehensively understand the therapeutic implications of this intriguing peptide.

Keywords: alamandine, allodynia, MrgD receptors, vlPAG, RVM

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Allogenic CAR-T cell therapy: challenges and perspectives (Review)

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Introduction: CAR-T cell therapy has emerged as a significant breakthrough in cancer treatments particularly in patients with hematological malignancies who have not responded well to previous therapies. Harnessing the power of the immune system to fight cancer is the basic concept of this treatment. the patient's T cells were genetically modified to express a synthetic receptor called chimeric antigen receptor. These receptors are designed to recognize certain molecules in cancer cells and eliminate them. Despite being a revolutionary approach, As mentioned above the source of engineered T-cells, are autologous. even though they have demonstrated remarkable clinical success, it is associated with several limitations including severe side effects, manufacturing time, cost, and feasibility issues for patients who lack adequate T-cell population. Allogenic CAR-T cells represent an alternative approach by utilizing healthy donor-derived T-cells instead of patient's derived ones. This innovative solution allows for wider accessibility and reduced manufacturing time compared to autologous therapies that require a personalized production process. Despite offering several advantages, allogenic therapy faces its limitations such as graft-verses-host-disease (GVHD). Effective application of this approach is due to overcoming these challenges. In this review, we investigate the viability of allogenic CAR-T cell therapy using double-negative T-cells (DN T cells) as the new cell sources for this novel therapeutic approach.

Methods: To identify relevant studies a comprehensive search of electronic databases such as Pubmed, Scopus, and Frontiers Immunology was conducted. The search terms used were "allogenic CAR-T cell therapy, double negative CAR-T cells(DN CAR-T cells), CAR-T cell therapy, and cancer treatment." The search was limited to articles published from 2012 to 2023. Studies were only included if they investigated allogenic CAR-T cell therapy using DN-CAR T cells. Studies that focused on autologous CAR-T cell therapy were excluded. Inclusion criteria also required studies to report safety, efficacy, and potential adverse events associated with DN-CAR T cells. The data extracted from included articles were summarized and analyzed to identify common themes across them.

Results: Double negative CAR-T cells are subset of T-cells that lack CD4 and CD8 co-receptors and express a chimeric antigen receptor on their surface. potential usage of these cells as sources for allogenic settings is due to several advantages they possess over autologous sources and conventional CAR-T cells. One of the major limitations of allogenic sources is the risk of GVHD, in which the donor T-cells attack the recipient's healthy tissues. However, DN T-cells, by lacking CD4 and CD8 co-receptors, that are crucial for T cell activation and subsequent GVHD development, can reduce the risk of GVHD. Based on the prior studies that were conducted on animal models, mice treated with DN CAR-T cells targeting CD19, showed an 80 percent survival rate after 120 days which proved their persistency. Furthermore, DN-CAR-T cells have demonstrated a lower potential for off-target toxicities compared to conventional CAR-T cells. This is attributed to their more limited repertoire of T-cell receptors and reduced expression of activation markers. DN CAR-T cells offer advantages in terms of scalability and manufacturing. conventional CAR-T cells cannot be pooled from different donors due to alloreactivity. However, DN T cells derived from various donors can be expanded in a single culture without losing their functionality. This facilitates large-scale production which is a crucial aspect of the clinical application of allogenic CAR-T cell therapy. In current allogenic approaches with conventional T-cells, genetic modifications such as TCR knockout are conducted to prevent GVHD. Despite the effectiveness of these strategies they complicate the process therefore DN T cells remain an attractive alternative.

Conclusion: Allogenic DN CAR-T cell therapy holds potential value in the future as to date it has minimized the challenges such as GVHD and severe side effects in previous approaches and simplified manufacturing process. Further research and clinical trials should focus on enhancing safety, exploring combinational approaches, and conducting long-term efficacy. By addressing these areas, Allogenic CAR-T cell therapy using DN-CAR-T cells can revolutionize the field of cancer treatment and broaden its application to both hematological malignancies and solid tumors.

Keywords: CAR-T cell therapy, double negative CAR-T cells, allogenic CAR-T cell therapy, cancer treatments

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Alterations in the plasma expression of mir-15b, mir-195 and the tumor-suppressor gene DLEU7 in patients with B-Cell chronic lymphocytic leukemia (Research Paper)

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Introduction: Chronic lymphocytic leukemia (CLL) is one of the most prevalent forms of leukemia in adults. Inactivation of the DLEU7 gene is frequently observed in patients with CLL. Furthermore, microRNAs (miRNAs) have been observed to have a critical role in the pathogenesis of several cancers, including leukemia. Considering the tumor-suppressive role of DLEU7, as well as the tumor suppressor or oncogenic role of microRNAs (miRNAs), the aim of the present study was to evaluate the potential miRNAs targeting the DLEU7 gene in B-cells and explore expression changes these genes in the plasma of B-CLL patients.

Methods: The miRNAs interacting with the DLEU7 gene were predicted and selected using bioinformatics tools. A total of 80 plasma samples were collected from 40 patients with B-cells and 40 healthy individuals, then subjected to RNA extraction and cDNA synthesis. The expression profiles of the predicted miRNAs and the DLEU7 gene in the plasma of B-CLL patients and healthy individuals were determined by RT-qPCR analysis.

Results: The bioinformatics prediction indicated that miR-15b and miR-195 target the DLEU7 gene. The expression levels of miR-15b and miR-195 were significantly higher in the plasma of patients with B-CLL compared to the healthy individuals (91.6, p= 0.001) (169, p= 0.001). However, the expression level of the DLEU7 gene was found to be significantly lower in the patient group compared to healthy controls (0.304, p= 0.001).

Conclusion: Both miR-15b and miR-195, have the potential to function as novel and non-invasive biomarkers in the diagnosis and prognosis of patients with B-CLL.

Keywords: B-CLL, miRNA, Biomarker, DLEU7, RT-QPCR.

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Ameliorative Effect of Zinc Oxide Nanoparticles on Daily Sperm Production and Sperm Parameters in Mice under Oxidative Stress Induced by Taxol (Research Paper)

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2.

Introduction: Infertility is a major concern for young men of reproductive age under-going chemotherapy. In general, chemotherapeutic agents target rapidly dividing germ cells, and thus lead to impairment of spermatogenesis and reduced sperm count in cancer survivors. This study investigated the effects of taxol on sperm parameters and oxidative stress and antioxidant properties of zinc oxide nanoparticles in adult male NMRI mice.

Methods: Mice were divided into control, taxol (5mg/kg), zinc oxide nanoparticles (5mg/kg) and taxol + zinc oxide nanoparticles groups and intraperitoneally treated for 35 days. Then, mice were anesthetized, and the caudal region of the left epididymis was used to measure the sperm parameters and the right testis to calculate the daily sperm production (DSP). Total antioxidant capacity (TAC), malondialdehyde (MDA) and serum testosterone levels were also measured. The data were analyzed by One-Way ANOVA and Tukey's test considering a significance level of $p<0.05$.

Results: A significant decrease in the mean count, motility, viability and DSP, testosterone and TAC levels was observed in the taxol group compared to the control group ($p<0.001$). While MDA level showed a significant increase in the taxol group compared to the control group. ($p<0.001$). The simultaneous treatment of zinc oxide nanoparticles with taxol significantly improved the mentioned parameters compared to the taxol group and brought them to the control level.

Conclusion: The findings of this study showed that Zinc oxide nanoparticles, due to its effective and potent antioxidant properties, could suppress the destructive effects of Taxol on sperm parameters.

Keywords: Taxol, Zinc Oxide Nanoparticles, Sperm, Oxidative Stress, Mice.

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Ameliorative Effects of Vitamin C and Methanolic Extract of Broccoli on Cyclophosphamide-induced Poisoning in Ovary of Rat (Research Paper)

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Introduction: Considering the importance of using herbal compounds to reduce the side effects of cyclophosphamide (CPH), the current study aimed to evaluate the effects of broccoli extract and Vitamin C on ovarian poisoning with CPH.

Methods: Four equal groups of 48 adult female Wistar rats were formed. The first group that was control received physiological saline orally without treatment. A 200 mg/kg dose of CPH was administered intraperitoneally to the second group. For the third group, CPH was supplemented with 300 mg/kg of Vitamin C, and methanol extract of broccoli 300 mg/kg was used in the fourth group. The serum total antioxidant capacity (TAC), interleukin-1 and tumor necrosis factor alpha (TNFα) and ovarian tissue glutathione peroxidase (GPx), superoxide dismutase (SOD), malondialdehyde (MDA), catalase (CAT), were measured. At the end of the study, the ovarian tissue was cut and stained for histopathological investigations.

Results: Ovarian tissue GPx, CAT, and SOD values indicated a significant decrease in the CPH group compared to other groups. In the CPH plus broccoli group, there was a significant decrease in MDA ovarian tissue and IL-1 and TNF-α in serum, compared to the CPH group. There were significant negative changes in ovarian cells of the CPH group, compared to the control and other treatment groups.

Conclusion: The current study suggested that administrating broccoli extract plus CPH could increase the superior antioxidant potential, compared to Vitamin C. This can potentially decrease CPH-induced damage to the ovary of rats, thereby improving their fertility status.

Keywords: Antioxidant, Broccoli extract, Cancer, Cyclophosphamide, Ovary, Vitamin C

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An effective breast cancer therapy based on CRISPR-Cas9 gene-editing tool (Review)

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Introduction: There are several factors that contribute to cancer, including genetic alterations to the cells and heterogeneous microenvironments. Cancer progression and resistance to therapy are primarily related to changes in the regulation of these genes, referred to as tumor suppressors and oncogenes. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) have shown a considerable improvement in terms of accuracy, efficiency, and specificity, which makes them very attractive over other nuclease-based tools. There has been a tremendous improvement in genome editing technologies, such as CRISPR-Cas9 systems, which are robust and programmable and have enabled genome editing to be used for cancer modeling and cancer treatment. It has been discovered that the CRISPR-Cas9 system can be exploited to discover new genes and introduce them into the gene therapy field as novel targets. It can be used as a powerful tool to introduce genes into the gene therapy field as Novel targets. The main objective of the present review is to summarize the capabilities and pitfalls of CRISPR-Cas9, as well as the potential applications for breast cancer treatment using this revolutionary technology.

Methods: Scopus, PubMed, ScienceDirect, and Google Scholar are some of the universally recognized databases used to retrieve published data from 2015 to 2020. CRISPR-Cas-based breast cancer treatment applications were the subject of the search strategy. Specific keywords such as “CRISPR/Cas”, “Cancer”, “Gene editing”, “Breast cancer”, and “Cancer therapy” were used. Specific keywords such as “CRISPR-Cas9”, “Cancer”, “Gene editing”, “Breast cancer”, and “Cancer therapy” were used. 1000 studies were funded. Based

on abstracts, 9700 studies were omitted, and 300 went for full reading texts. Fifty relevant articles with complete abstracts were included in the study.

Results: Mutations in the tumor protein 53 (TP53) are found in most tumor cells. In response to internal stresses and abnormalities, p53 suppresses cell proliferation and encodes the tumor suppressor protein. Oncogene H-Ras expression in a xenograft model was shown to induce cellular transformation through CRISPR/Cas9-mediated deactivation of Transformation Related Protein 53 (TrP53). Alternatively, studies employed the CRISPR-Cas9 system to target oncogene Human Estrogen Receptor 2 (HER2). Breast cancer cells with Her2-positive exons 5, 10, and 12 found that co-expression of Cas9 and three sgRNAs reduced both cell growth and tumorigenicity. There is a strong relationship between CRISPR-Cas9 down-regulation of HER2 and the reduction of cancer risk rather than conventional therapies such as monoclonal antibodies (mAbs) mainly due to the possibility of designing new guide RNAs that could target new mutations if resistance develops. Glycoprotein epidermal growth factor receptors have an intracellular tyrosine kinase domain and are attached to cells' membranes. Mutations in the genetic code cause constitutive activation of the tyrosine kinase receptor, and this leads to the development and progression of cancer. The most effective therapies for EGFR-expressing cancers are Tyrosine Kinase Inhibitors (TKIs). However, resistance to these medications develops within two years. CRISPR-Cas9 nickase platform has been proposed by studies to repair mutated EGFR using molecular surgery through the CRISPR system. Researchers have recently been able to target epigenetic irregularities using the CRISPR-Cas9 system due to its ability to shed light on current epigenetic irregularities. As well as oncogenes encoded by viruses, the CRISPR process can be used to eliminate them.

Conclusion: CRISPR-Cas9 could be a game-changer for cancer treatment in the future thanks to its advantages over other genome editing techniques. The goal can be achieved through the use of CRISPR-Cas9 as an effective gene therapy tool and the identification of biomarkers that are prognostic and predictive, as well as of novel targets and pathways for signaling in breast cancer, as well as the development of new drugs. There are limitations and cautions associated with CRISPR-Cas9 that must be considered before using this tool for determining novel immune system-tumor interplays and enhancing cellular immunotherapies.

Keywords: Breast cancer, Cancer, CRISPR-Cas9, Gene-editing

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An experimental study about The Role of Interferon Beta (IFN-β) in the Treatment of Multiple Sclerosis (MS) (Research Paper)

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system. Interferon beta (IFN-β) has been used as a treatment for MS for over two decades, but its mechanism of action is not fully understood. In this study, we aimed to investigate the role of IFN-β in the treatment of MS using a mouse model.

Methods: We used more than 50 mice with experimental autoimmune encephalomyelitis (EAE), a mouse model of MS. The mice were divided into two groups: one group received IFN-β treatment, while the other group received a placebo. We monitored the mice for clinical signs of EAE and assessed the severity of the disease using a scoring system.

Results: Our results showed that IFN-β treatment significantly reduced the severity of EAE in mice compared to the placebo group. The IFN-β-treated mice had lower clinical scores, reduced inflammation in the central nervous system, and decreased demyelination compared to the placebo group.

Conclusion: Our study suggests that IFN-β has a beneficial effect on the treatment of MS by reducing inflammation and demyelination in the central nervous system. These findings provide further support for the use of IFN-β as a treatment for MS.

Keywords: Multiple sclerosis, autoimmune disease, Interferon Beta

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An insight to immunotherapy methods and its challenges (Review)

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Introduction: So far, cancer treatments such as surgery, chemotherapy, and radiotherapy have been utilized to remove or directly attack cancer cells. However, these treatments are often ineffective for advanced or recurrent stages of cancer. To address this, cancer immunotherapy has been proposed as the fourth cancer treatment. This type of therapy includes monoclonal antibodies, immune checkpoint blockers, cancer vaccines, and cell-based therapies, which have proven to be effective. While immunotherapies have revolutionized the future of treatment for various solid and hematologic malignancies, they also present unique toxicity profiles that vary depending on the type of immunotherapy used. Recent clinical studies have revealed that patients who respond to immunotherapy have longer survival rates with less metastatic recurrence, indicating that immunotherapy may be a solution to overcome cancer metastasis. However, there are limitations and challenges associated with this method of treatment. In this article, we will explore the different types of immunotherapy mentioned above and the obstacles of this type of cancer treatment. ICIs are monoclonal IgG antibodies that work by interrupting inhibitory signals that deactivate cellular immune effector cells. Immune checkpoints play a role in limiting the immune response and promoting self-tolerance by deactivating cytotoxic T-cells. By disrupting the interaction between immune checkpoints and cancer cells, ICIs keep T-cells activated and enable them to target cancer cells. Ipilimumab was the first immune checkpoint inhibitor (ICI) to be approved by the FDA in 2011 for the treatment of advanced melanoma. Clinical trials for multiple types of cancer have demonstrated that checkpoint inhibitors have favorable outcomes in both tumor regression and patient survival. However, non-specific immunostimulation caused by ICIs may lead to organ-specific inflammation, tissue damage, and autoimmunity, resulting in unique adverse effects.

Methods: The use of immune checkpoint inhibitors in clinical practice has significantly progressed cancer treatment. Nevertheless, their efficacy is restricted as tumor cells employ diverse mechanisms to evade antitumor effects. To overcome these mechanisms and enhance the adaptability of current cancer immunotherapies, it is crucial to gain a more comprehensive

understanding of the TME and devise innovative approaches, such as cancer vaccines. We anticipate that this review will encourage further advancements in cancer immunotherapies One vaccine strategy being examined is an autologous tumor cell vaccine that employs a patient's cancer cells. This approach involves administering irradiated tumor cells with an adjuvant. Since this vaccine utilizes tumor cells, it has the potential to generate T cells that are specific to any antigen expressed by the cells used. However, the challenge with this strategy is that obtaining a sufficient number of cells can be difficult. This method has been tested in numerous tumors, including lung cancer, colorectal cancer, melanoma, renal cell carcinoma, and prostate cancer. Within the tumor microenvironment (TME), various cytokines are necessary for immune cells to sustain their growth, activation, and ability to infiltrate tumor regions. Specifically, administering IL-2 has demonstrated notable antitumor effects and reduced metastatic tumor progression in murine tumor models. In 1992, the FDA approved IL-2 therapy for the treatment of renal cell carcinoma and melanoma, with response rates ranging from 15% to 29% across different studies.

Results: Successful anti-cancer immune response requires multiple processes that are often compromised during tumor progression. Single-agent immunotherapy has limitations, and combining it with different steps of immunosurveillance may restore anti-tumor immunity. Defining immune profiles using biomarkers may reveal more efficient combination therapies. Current and future immuno-oncology will expand the frontiers of immunotherapy and benefit more cancer patients.

Conclusion: Immunotherapy has demonstrated encouraging outcomes in treating resistant cancer histologies. Despite this, its advantages are still constrained due to low response rates in certain tumor types and variations in response among different tumor lesions. Resistance to immunotherapy can arise from a variety of factors, including genetics, metabolism, inflammation, and abnormal neovascularization. Research is being conducted to identify and comprehend these mechanisms of resistance in order to enhance cancer diagnosis and treatment for personalized care. Harnessing and renormalizing immune responses in cancer patients has led to new cancer immunotherapies.

Keywords: Immunotherapy, immune checkpoint inhibitor, cancer vaccine

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An overview of the impact of blood-based DNA methylation signatures in breast cancer diagnosis (Review)

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Introduction: Changes in DNA methylation patterns play a significant role in carcinogenesis, and sensitive epigenetic signatures principally controlled by DNA methylation, regulate the interaction between genetic and non-genetic risk factors through carcinogenesis. These alterations may be presented in blood DNA, which is a non-invasive method for breast tumor analysis. blood-DNA detection objects principally included circulating cancer DNA/cell-free DNA (ctDNA/cfDNA), circulating cancerous cells (CTCs), and exosomes. Researches gradually showed that methylation changes in peripheral blood mononuclear cells (PBMCs) also can be responsible for the manifestation of cancers.

Methods: we searched articles by keywords such as: breast cancer, DNA methylation, immune and peripheral blood mononuclear cells (PBMCs) in PubMed and Google Scholar. Then, related papers that coordinated such word criteria were precisely reviewed and their findings duly noted.

Results: The present study offers brief research on DNA methylation changes in breast cancer and describes the characteristics of blood-based DNA detection objects including: ctDNA/cfDNA, CTCs, exosomes, and PBMCs and their utilization in medical tests especially for early detection of breast cancer.

Conclusion: The use of blood-based DNA requires more studies to be able to use diagnostic kits with high sensitivity and specificity to detect this disease in the early stages.

Keywords: breast cancer, DNA methylation, circulating tumor cells and peripheral blood mononuclear cells(PBMC)

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An Overview on Applications of Exosome-Loaded Hydrogels as New Class of Biomaterials for Tissue Engineering (Review)

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Introduction: Background: Exosomes are nanometer extracellular vesicles that have found many applications in drug delivery and tissue engineering. However, the need for a carrier for their targeted local release is very felt. On the other hand, considering the biocompatibility and many applications of hydrogels in tissue engineering, it seems that the use of exosome-containing hydrogels can be a new approach in the construction of scaffolds for use in various tissue engineering.

Methods: Materials and Methods: In this review, PubMed, ISI Web of Science, Google scholar and SCOPUS databases were searched for studies published up to September 2023 related to “An Overview on Applications of Exosome-Loaded Hydrogels as New Class of Biomaterials for Tissue Engineering” were addressed.

Results: Results: The review of studies shows that due to the presence of many bioactive factors in exosomes, as well as their favorable local release and other advantages of hydrogels, such as their use in the preparation of injectable biomaterials, hydrogels loaded with exosomes are widely used. They are found in wound healing, bone tissue engineering, and nerve regeneration. In this study, an attempt has been made to review some of the mentioned systems.

Conclusion: Conclusion: The conclusion of the study shows that exosome-loaded hydrogels can create a new generation of biomaterials for new tissue engineering applications.

Keywords: Keywords: Exosomes, Hydrogels, Scaffolds, Regenerative Medicine.

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Angiogenesis and Therapeutic Implications in Liver Cancer: Mechanistic Insights and Future Perspectives (Review)

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Introduction: Liver cancer, predominantly hepatocellular carcinoma, represents a major cause of cancer-related mortality worldwide. Angiogenesis, driven by a complex interplay of pro-angiogenic and anti-angiogenic factors, plays a pivotal role in the pathogenesis of liver cancer. The dysregulation of angiogenesis contributes to tumor growth, vascular invasion, and distant metastasis. Consequently, understanding the molecular mechanisms underlying angiogenesis in liver cancer is crucial for the development of novel therapeutic approaches. . Understanding the underlying mechanisms of angiogenesis in liver cancer is essential for the development of effective therapeutic strategies. This review article aims to provide a comprehensive overview of the mechanisms involved in angiogenesis in liver cancer and highlight the therapeutic perspectives targeting angiogenesis in liver cancer treatment.

Methods: A comprehensive search was conducted using electronic databases such as PubMed, Embase, and Web of Science to identify relevant studies investigating angiogenesis in liver cancer. The search strategy included keywords such as "angiogenesis," "liver cancer," "hepatocellular carcinoma," and "therapeutic strategies." Selected studies were thoroughly reviewed and analyzed to elucidate the mechanisms and potential therapeutic targets associated with angiogenesis in liver cancer.

Results: The results section presents the key findings related to the mechanisms driving angiogenesis in liver cancer. Several angiogenic factors, including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF), contribute to the formation of new blood vessels in liver tumors. The activation of signaling pathways such as the VEGF receptor pathway, the Wnt/β-catenin pathway, and the PI3K/Akt/mTOR pathway regulates angiogenesis in liver cancer. Moreover, the role of tumor microenvironment components, including immune cells and hepatic stellate cells, in promoting angiogenesis is discussed. Additionally, the section highlights potential therapeutic strategies targeting angiogenesis in liver cancer, such as anti-angiogenic agents, multi-kinase inhibitors, and immune checkpoint inhibitors.

Conclusion: Angiogenesis plays a critical role in liver cancer development and progression. Understanding the complex molecular mechanisms involved in angiogenesis provides valuable insights into potential therapeutic targets. Targeting angiogenesis has emerged as a promising strategy for liver cancer treatment, with anti-angiogenic agents and other targeted therapies showing promise in preclinical and clinical studies. However, further research and clinical trials are necessary to optimize these therapeutic approaches and improve patient outcomes in liver cancer.

Keywords: Angiogenesis, liver cancer, hepatocellular carcinoma, molecular mechanisms, therapeutic strategies.

Angiogenesis in Colorectal Cancer: Mechanisms and Therapeutic Perspectives (Review)

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Introduction: Colorectal cancer is a major public health issue with high morbidity and mortality rates. Angiogenesis, regulated by various factors including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF), is essential for tumor growth, invasion, and metastasis. Understanding the intricate molecular pathways involved in angiogenesis in CRC is crucial for the development of effective therapeutic strategies.

Methods: A systematic literature search was conducted using electronic databases such as PubMed, Embase, and Web of Science. The search strategy included keywords such as "angiogenesis," "colorectal cancer," "molecular mechanisms," and "therapeutic strategies." Relevant articles published between 2000 and 2023 were considered. The selected studies were critically evaluated and analyzed for their contributions to understanding angiogenesis in CRC.

Results: The results section highlights the key findings related to the mechanisms driving angiogenesis in CRC. Multiple pathways, including the VEGF pathway, the Notch signaling pathway, and the transforming growth factor-beta (TGF-β) pathway, have been implicated in promoting angiogenesis in CRC. Tumor cells, endothelial cells, and the tumor microenvironment play a collaborative role in enhancing angiogenesis through the secretion of angiogenic factors and the recruitment of immune cells. Moreover, the section provides an overview of preclinical and clinical studies investigating therapeutic strategies targeting angiogenesis in CRC, such as anti-angiogenic agents, tyrosine kinase inhibitors, and immune checkpoint inhibitors.

Conclusion: Angiogenesis is a critical process in CRC development and progression. Targeting angiogenesis has emerged as a promising therapeutic approach in CRC treatment. The understanding of the complex molecular mechanisms driving angiogenesis in CRC provides valuable insights into potential therapeutic targets. Various anti-angiogenic agents have demonstrated efficacy in preclinical and clinical studies, either as monotherapy or in combination with standard treatments. However, further

research and clinical trials are needed to optimize these strategies and improve patient outcomes in CRC.

Keywords: Angiogenesis, colorectal cancer, molecular mechanisms, therapeutic strategies, anti-angiogenic agent

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Animal ethics in Biology labratory (Research Paper)

Faezeh Sadat Kermani,[1,*]

1. Islamic Azad university of Roudehen

Introduction: In this essay i would like to speak about animal testing that found to how affected to the humans health

Methods: Some company use another way replace this for example they use computers data or human testing and another in anyway the ethicet is so important to them on top of that we should try to dont destroyed our environment and do our best about treat a good with it

Results: Lets begin by looking the computers data today the technology is progress more and more Computing techniques such as machine learning can translate animal data to human data and integrate data from multiple human clinical trials. Ultimately, computer models are not just a more humane alternative to animal studies; they are potentially “faster, cheaper, and more accurate,”

Conclusion: we should respect to animals

Keywords: animal testing

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Animal testing and cosmetics (Research Paper)

Faezeh Sadat Kermani,[1,*]

1. Roudehen Islamic Azad University

Introduction: In this article i discussed animal testing and the suffering of animals and alternative methods with non violent

Methods: some company use another way such as 1 3D tissue culture also referred as organs on a chip 2 stem cell research 4 mathematical models

Results: we can use another way too keep animals and environment for better future

Conclusion: animal studies fail to 50 percent of cases and we need to use another tests

Keywords: peta.org

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Anti proliferative potential of the phenolic compounds from olive leaves on both HER2 positive and HER2 negative breast cancer cells (Research Paper)

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Introduction: Considering increasing rate of in the incidence and mortality of breast cancers, increasing concerns arisen to find safer alternative approaches for conventional clinical treatments include chemotherapy or radiotherapy mainly due to their deleterious side effects and high cost. Herbal-derived ingredients such as phenolic compounds are of major interest In the continuous search for safer and more effective treatments. Present study aimed to assess anticancer, anti-inflammatory and antimicrobial capability of extracted poly phenols from olive leaves on both HER2 positive and negative breast cancer cell lines MCF7 and MDA231.

Methods: For the initial extraction of polyphenolic compounds, fresh and green olive leaves were powdered, lysed with water and ethanol (70:30) through sonication for 15 minutes. Its total antioxidant property was measured using the DPPH method. The biological effect of phenolic extract on normal cells and breast cancer cell lines was measured by MTT assay.

Results: The results demonstrated that phenolic extract inhibited cells survival in a dose and time dependent manner. Further, the superior antioxidant properties of phenolic compounds were found in specific concentrations compared to the standard sample of ascorbic acid.

Conclusion: It was concluded that obtained phenolic extract of olive leaves has a great potential to be used as anticancer agent due to its significant effect on inhibition of cell proliferation, growth and viability in breast cancer cells.

Keywords: phenolic compounds, olive leaf, breast cancer, antioxidant, anticancer drugs

Anti-inflammatory and Immunomodulatory Effects of Mesenchymal Stem Cell Therapy on Parasitic Drug Resistance (Review)

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Introduction: Increasing antiparasitic resistance poses a threat to the lives of humans and animals in today's world. In spite of the limited variety, these medicines have been extensively used to treat humans, pets, and food animals. These medicines become less effective as a result of resistance, necessitating alternative treatment approaches. Mesenchymal stem cells (MSCs) have shown promise as a potential therapy for parasitic infections. A number of parasitic infections have been treated with MSCs, including malaria, schistosomiasis, cystic echinococcosis, trypanosomiasis, toxoplasmosis, and leishmaniasis. The prevalence of parasites decreased under MSC therapy. In this way, MSCs may directly combat parasitic infections by preventing parasite survival and proliferation. An examination of the medical literature regarding MSCs and antiparasitic properties will be presented in this review. Despite this being an emerging field of research, we will outline possible mechanisms as well as examine the potential synergy between combination therapies and their possible dangers.

Methods: An extensive search was conducted in nine databases from January 2000 to January 2023 in order to locate published articles on Mesenchymal Stem Cells' anti-inflammatory and immunomodulatory effects on Parasitic Drug Resistance. There were 10,000 studies funded based on search terms such as Mesenchymal stem cells, anti-inflammatory, immunomodulatory, parasite drug resistance, and immunotherapy. We excluded 9700 articles solely based on abstracts of the articles, while we read all 300 articles in their entirety. The study included 50 relevant articles with complete abstracts, which were included in the analysis.

Results: Using MSCs for the treatment of parasitic infections was examined in this study based on the most recent preclinical studies. The current study summarized empirical findings on the effects of MSC therapy against parasitic infections. Study findings indicate that administering MSCs reduces the prevalence of parasites such as toxoplasmosis, schistosomiasis, malaria, cystic echinococcosis, leishmaniasis, and trypanosomiasis in patients with these infections. Cytokines that stimulate or inhibit inflammation are modulated by it. Furthermore, the anti-parasitic and immunomodulatory properties of MSCs were improved by their administration with anti-parasitic medications. Inhibition of fibrosis caused by MSCs and their use successfully in infectious disease therapy suggest that MSCs could be effective in treating S-japonicum infection and may allow a better understanding of how MSCs affect disease mechanisms. Plasmodium infection is prevented by malaria's MSCs since they modulate immune responses and reprogram erythropoiesis. Hepatogenic differentiation potential, immunomodulatory properties, and the ability to secrete trophic factors make BM-MSC transplants a promising alternative to liver regeneration. Due to the role the immune system plays in the physiopathology of Chagas disease, BM-MSC may be an effective cell type for treating Chagasic cardiomyopathy. It has been found that human BM-MSCs are more effective at eliminating toxoplasma gondii than mouse BM-MSCs, which require pretreatment with IFN-, TNF-, and IL-1 before they can be effective at eliminating toxoplasma gondii. A cell-based assay revealed promising immunomodulatory results from L-major (related to the visceral form).

Conclusion: A synergistic effect was observed with MSCs in combination with conventional antiparasitic medications. The researchers discovered that these medications were enhanced by combining them with MSCs. It is, therefore, likely that MSCs may enhance the efficacy of antiparasitic drugs, ultimately leading to improved therapeutic results. Therefore, the combination of MSCs with anti-parasitic medications holds great promise for both the prevention and treatment of parasitic diseases. In addition to reducing parasite prevalence and modulating the immune response, MSC therapy is effective as an adjunct treatment strategy. MSCs must be further researched and tested in clinical trials in order for their safety and efficacy to be validated. This study offers a convincing starting point for more research on parasitic diseases and hopes for more effective interventions for the protection of both humans and animals.

Keywords: MSC, Parasitic, Mesenchymal Stem Cell, Infection, Malaria

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Anti-Inflammatory Effect of Bevacizumab in Rat Model of Asthma
(Research Paper)

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Introduction: Asthma, a highly prevalent condition, involves factors such as inflammation, airflow obstruction, elevated bronchial blood pressure, and external conditions. The clinical symptoms predominantly revolve around smooth muscle contraction and inflammation, leading to airway constriction and obstruction. A variety of stimuli, including respiratory infections, allergic reactions, irritants, exercise, and non-steroidal anti-inflammatory medicines, contribute to bronchial blockage. Bevacizumab, a humanized anti-VEGF monoclonal antibody recognized for its role in inhibiting angiogenesis, finds application in the treatment of various malignancies.

Methods: A study involving twenty-one male Wistar rats distributed across three randomized groups – control, ovalbumin (OVA)-sensitized, and OVA+Bmab – was conducted. OVA and OVA+Bmab groups underwent sensitization to ovalbumin (OVA) and aluminum hydroxide on days 1, 5, and 10, followed by a 14-day challenge with atomized OVA (inhalation). The OVA+Bmab group received Bevacizumab post-OVA sensitization for two weeks. Finally, in day 47 all of the rat groups were sacrificed. The study evaluated gene and protein expression of type 2 T-helper cell-like cytokines (IL-4, IL-5, IL-13), goblet cell population, inflammatory cell population, VEGF, and allergen-specific IgE in bronchial alveolar lavage fluid (BALF).

Results: Bevacizumab effectively mitigated bronchial inflammation by reducing type 2 T-helper cell-like cytokines ($p \leq 0.05$). Additionally, the OVA-specific-IgE level significantly decreased in the OVA+Bmab group. Furthermore, the OVA+Bmab group exhibited significantly reduced numbers of macrophages, neutrophils, and lymphocytes compared to the OVA group ($p \leq 0.05$).

Conclusion: The study underscores the significance of VEGF in generating inflammatory mediators within lung airways during asthma. Addressing VEGF via anti-VEGF agents like Bevacizumab holds promise as a therapeutic avenue for enhancing asthma management.

Keywords: Bevacizumab, bronchial alveolar lavage fluid (BALF), asthma, inflammation

Antibacterial effects of carbon dots in medical systems (Research Paper)

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Introduction: Infections caused by fungi, bacteria, parasites, or viruses cause many severe diseases. Antibiotics have historically been the primary weapon in the fight against infectious diseases. However, due to the high cost and long pathways to new drugs discovery, clinical testing, and scaling up the production process, approval of the development of next- generation antibiotics takes longer. As a result of multidrug resistance (MDR), which is of particular concern for high- risk populations such as those in healthcare settings or for those with concurrent conditions, such as cancer, bacterial infections can severely worsen patient health; infections may also delay wound recovery even when treated, with some negative health impacts associated with current disinfection techniques many of these diseases will become more challenging to treat and result in higher medical costs and mortality rates. Photodynamic inactivation of bacteria mediated by photoactive compounds, more precisely photosensitizer molecules (PSs), is one of the most promising techniques in the fight against MDR pathogens. Photodynamic antimicrobial chemotherapy (PACT) is a fast, intense and challenging field that has been developed to address the growing antibiotic resistance among harmful bacteria. Carbon dots (CDs) have been proposed as a potential fluorescent nanomaterial for identifying and inactivating different types of bacterial species among a wide variety of PSs, already used in the past. They have good photoelectric properties, high water solubility, and chemical durability. CDs also present low toxicity and have good biocompatibility, making them ideal for photocatalytic dye degradation, photocatalytic/electrical water splitting, solar devices, bioimaging, drug delivery, gene delivery, biosensors and fluorescent-labeling applications and even in LED technologies.

Methods: Top-down and bottom-up approaches are two commonly used approaches for preparing CDs. Chemical processes such as hydrothermal, pyrolysis, combustion, ultrasonic, microwave irradiation, thermal, and biogenic procedures, conversely, are used in the bottom-up approach. Using a top-down technique, large-sized carbon materials, such as carbon nanotubes and graphite ash, are decomposed into small CDs, from the macro to the

nanoscale. Different carbon sources are exposed to laser ablation, arc discharge, plasma treatment, chemical oxidation, electrochemical oxidation, and others. Although many of the aforementioned synthesis methods can be found in the literature, hydrothermal treatment in either a top-down or bottom-up regime is most commonly employed. In particular, this method is favored amongst reports of carbon dot “green synthesis” from biomass, or natural precursors. Currently, the main green synthesis processes for producing CDs include ultra-sonication, microwave irradiation, hydrothermal carbonization, self-exothermic synthesis, and ozone/hydrogen peroxide oxidation. For the green synthesis process, toxic chemicals that are harmful to people’s health and the environment should be avoided.

Results: Thus far, much work has been performed on the cytotoxicity of CDs on mammalian cells, and it has been reported that they are non-toxic at proper concentrations both in vitro and in vivo. A high concentration of CDs will exert toxic effects on the central nervous system. Toxicology reports of GQDs indicate that although most existing studies support the safe use of GQDs, their toxicity may vary depending on the concentration and test method used in the synthesis technology. Studies have found that small-sized CDs are more toxic than large-sized CDs, and CDs with negative charged are more cytotoxic to mammalian cells. In order to solve the above problems, it is necessary to promote safe and controllable CDs synthesis strategies and application methods, and the safe application of CDs in the treatment of infectious diseases requires in-depth research on its possible toxic side effects and complications.

Conclusion: The CDs’ structure work as a photosensitizer in PACT is discussed in many aspects and applications in this paper. CDs have been shown to be one of the most promising carbon classes of material to work properly as an antibacterial material because of their excellent physical and chemical properties, optical qualities, and photophysical and photochemical behavior associated with exceptional water solubility. Conversely, CDs face some problems, limiting their practical application. The exact process of photoluminescence is unknown, and CDs with extended excitation and emission wavelengths are still uncommon, leading to complex tissue and biofilm penetration. Second, relatively few CDs have intrinsic microbe targeting ability, resulting in a significantly reduced antibacterial effect that is essential in developing antibacterial CDs. Finally, CDs’ water solubility and biocompatibility influence their microbial therapy usage.

Keywords: Carbon dots, Photodynamic antimicrobial chemotherapy, Multidrug resistance, Photosensitizer

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Antibacterial Effects of Essential Oils of Lavandula and Rosemary on Staphylococcus aureus: In vitro and Animal Model (Research Paper)

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Introduction: Infectious diseases are one of the most common diseases around the world which impose enormous financial burden on society. Staphylococcus aureus is an important cause of nosocomial infections and multidrug resistance. Although synthetic antibiotics have been able to play an important role in treatment of infectious diseases in past decades, however problems related to microbial resistance of antibiotics have caused that the medical plants to be considered as an alternative.

Methods: In this study, essential oil was prepared from dried leaves of the Lavandula angustifolia and Rosmarinus officinalis, then anti-bacterial activities of the essential oil for Staphylococcus aureus was experimented, first by the method of well diffusion in agar, and later the amount of the MIC and MBC of the essential oils were measured by broth dilution method. In animal model study, first 5×105 CFU/ml of bacteria was intraperitoneally injected and after 24 hours, 0.5ml (as MBC concentration of each the essences) of essential oils, to female BALB/c mice was intraperitoneally injected. Then, the counting of bacterial colonies in spleen were determined with cultivation on Mueller Hinton agar after 7 days as the standard protocol.

Results: The experiment results concerning the determination of growth inhibition diameter in agar showed that the maximum of growth inhibition diameter is related to the essential oil of Lavandula angustifolia (30 mm), and the minimum of growth inhibition diameter is related to essential oil of Rosmarinus officinalis (10 mm) at the highest concentration (400 mg/ml). In conditions of in vivo, spleen supernatant cultivation, the average number of bacteria for Lavandula angustifolia and Rosmarinus officinalis essential oil were 2×102 CFU/ml and 6×102 CFU/ml respectively. These results showed significantly decrease in number of bacteria in all experimental groups ($p<0.5$) compared to control group.

Conclusion: In general, the results of evaluations in experimental conditions and the animal model showed that the essential oils of Lavandula angustifolia and Rosmarinus officinalis have the effective antibacterial activity against mentioned bacteria and can be useful to treatment of nosocomial infections.

Keywords: Antimicrobial, Lavandula angustifolia, Rosmarinus officinalis, Staphylococcus aureus.

Antibiotic Resistance and the MRSA Problem (Review)

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Introduction: Antibiotics are used to treat a number of infections caused by Staphylococcus aureus. The key bacterial processes that are targeted by a number of antibiotics used to treat staphylococcal infections include cell wall formation, translation, transcription, and DNA synthesis. Antibiotic resistance, however, is an issue that is getting worse, and unsuccessful treatments have high costs in terms of both money and lives. A large number of mobile genetic elements contribute to the spread of antibiotic resistance. These elements include altered drug targets, enzymatic drug inactivation, enhanced efflux of antimicrobial chemicals, and altered drug accessibility. Although almost all compounds have shown resistance, specific strains resistant to all medications have not yet been identified. Yet resistance still poses treatment challenges, as exemplified by vancomycin. The aim of this study was to investigate Antibiotic Resistance and the MRSA Problem.

Methods: With the title "Antibiotic Resistance and the MRSA Problem," this review study has been created using information from scholarly databases like Science Direct, Springer, Google Scholar, and PubMed.

Results: A notable feature of most MRSA isolates is that resistance to beta-lactams is expressed in a heterogeneous manner. For these strains, populations arising from a single cell display widely different resistance levels, with the majority of cells exhibiting a low level of resistance and a minority of cells being highly resistant. While some HA-MRSA isolates exhibit high-level, homogeneous methicillin resistance, CA-MRSA isolates often exhibit low-level, heterogeneous resistance. Insight into the molecular mechanisms underlying this phenomenon has come from the identification of mutations that convert strains expressing low, heterogeneous resistance into homogeneous, highly resistant strains. These mutations map to genes associated with cellular stress responses, such as stringent response signaling via ppGpp and the ClpXP protease controlling the Spx stress response indicating a close link between bacterial physiology and resistance levels. Despite the fact that MRSA strains have become resistant to beta-lactams through acquisition of one specific resistance determinant, the mecA gene, clinical MRSA isolates exhibit highly variable levels of resistance: in some MRSA strains resistance is barely above that displayed by susceptible isolates (methicillin MICs <3 µg/ml), while other strains are highly resistant

(methicillin MICs up to 1,600 µg/ml). The mechanisms underlying these intriguing differences in resistance level remain poorly understood. In some cases, high resistance levels were attributed to increased expression of PBP2a due to duplication or enhanced transcription of the mecA gene. Two functionally similar two-component systems, BlaR1/BlaI and MecR1/MecI, control transcription of mecA in response to beta-lactams, and because genetic mutations are common in the regulatory elements controlling mecA expression, the PBP2a level varies widely between MRSA strains. In several cases differences in resistance levels did not correlate to PBP2a expression, suggesting that factors other than PBP2a modulate the strain-specific level of beta-lactam resistance. Indeed, genetic screens have identified a number of auxiliary factors (also designated “fem- factors”) essential for methicillin resistance that are critical for PBP2a-mediated resistance to beta-lactam antibiotics. Examples include cell division proteins, native PBPs, and enzymes involved in the synthesis of teichoic acids and peptidoglycan precursors. In some cases, the requirements for these auxiliary factors have been explained. For example, the essential glycosyltransferase domain of the native PBP2 is needed to cooperate with the transpeptidase activity of PBP2a in the building of peptidoglycan.

Conclusion: Since medications that block the actions of auxiliary factors operate in conjunction with beta-lactams to kill MRSA, the fact that beta lactam resistance depends on them offers up new therapeutic options for MRSA infections.

Keywords: beta lactam, Antibiotic Resistance, MRSA

Antibody engineering of Edrecolomab to increase affinity with B7-H3 antigen in colorectal cancer treatment (Research Paper)

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Introduction: Colorectal cancer (CRC) is the second leading cause of cancer death worldwide. The majority of CRC cases and deaths attributable to modifiable are caused by risk factors, including diet (29%), physical inactivity (16%), alcohol intake (13%), smoking (11%), and excess body weight (5%) [1]. Angiogenesis also plays an important role in the occurrence and development of CRC[2]. in which VEGFA is a key driver of angiogenesis that is secreted from many types of cells including malignant cells [3]. B7-H3, an important immune checkpoint molecule, was highly expressed in CRC tissues and was involved in immune escape and tumor progression[4]. Targeting angiogenesis is an effective therapeutic strategy for various malignancies, including CRC[5]. Edrecolomab (monoclonal antibody 17-1A) is a murine monoclonal antibody that represents a novel therapeutic approach and has the potential to become a treatment of choice as monotherapy in colon cancer and in combination with chemotherapy colon cancer[6]. Edercolomab has been shown to have improved efficacy and safety in the treatment of various types of cardiovascular, cancer, respiratory, hematology, autoimmune diseases, and infections[7]. Antibodies (Abs) are glycoproteins belonging to the immunoglobulin (Ig) superfamily that are secreted by B cells to identify and neutralize foreign organisms or antigens. monoclonal antibodies (MAbs)comprise two heavy and two light chains and are grouped into different isotypes dependent on which type of heavy chain they contain. Therapeutic monoclonal Abs (mAbs) are typically of the γ-immunoglobulin (or IgG) isotype [8] structural bioinformatics methods such as homology modelling, protein–protein docking or protein interface prediction are already used for rational antibody design[9]. In this research, by designing a monoclonal antibody and examining its affinity with B7-H3 antigen, we were able to introduce it as an effective therapeutic candidate, in order to reduce angiogenesis in colorectal cancer.

Methods: Edrecolomab monoclonal antibody was obtained from NCBI database at http://www.ncbi.nlm.nih.gov and as well as from Protein Data Bank with PDB ID at https://www. rcsb.org/ was used. The sequence of light

and heavy chain with access code M15047.1 Mouse Ig gamma active m RNA from hybridism 17-1A/ as heavy chain and M15046.1 Mouse Ig kappa active m RNA from hybridism 17-1A. chain was selected as light source and antigen sequence with GI access code: 427931085. he proABC is a web server for predicting the residues in antibody-binding site, which are involved in antigen recognition (http://www.biocomputing.it/proABC). Checking functional amino acids in protein with A Bodybuilder software, the best formats for VH and VL parts can be checked separately [10]. predicted based on solvent accessible surface areas, a new scale for interface propensities, and a cluster algorithm to locate surface exposed areas with high interface propensities with InterProSurf software from our web server at http://curie.utmb.edu/prosurf.html. [11] SIFT server were used to predict (http://sift.jcvi.org/) whether an amino acid substitution affects protein function. [12] Docking was performed using HADDOCK 2.2/. This scrutiny was used to determine the interaction and orientation between the two molecules to determine the correct binding between the antigen and the antibodies at http://haddock.science.uu.nl/services/HADDOCK 2.2 [13].

Results: HADDOCK software is a docking method based on the information of complex biomolecule models advances its information based on protein-protein face-to-face regions [14] After these steps, the structures are classified with the reported software and the best structure is classified in the first cluster. The highest score given by the software represents the affinity of the antibody with the antigen, which was assigned to variant 13 here. Cluster size from the clustering algorithm is an accurate and scalable method for detecting and predicting protein complexes in a network [15]. identification of repeats and motifs to understand their function at the level of a protein sequence is created by RSMD [16] electrostatic force occurs even before direct protein-protein contact is formed, may cause complex formation [17]. The protein-protein interaction is, in particular, the relationship between the area and the chemical nature of the interaction in binding the antibody to the antigen [18].

Conclusion: According to the results of molecular docking, it showed the binding affinity of Edercolomab antibody and engineered B7-H3 antigen, which was obtained from the reaction between the ligand and the binding site of the antibody. Edercolomab may inhibit the Angiogenic factor of VEGF and can be a good candidate for colorectal cancer treatment.

Keywords: antibody monoclonal, antigen, Angiogenic factor

Anticancer Activity of cobra venom componeuts against cancer (Review)

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Introduction: While the survival has increased due to treatment for cancer, But it has many side effects. cancer is the most common disease among men and women. for example Hepatocellular carcinoma is the most common cancer in adults. anticancer activity effect on Hepatocellular with gel filtration chromatography cobra venom in 2021. This review article the important role of cobra venom that researchers can investigated in cancer treatment. Cancer is the most problem over the world(1). 25% of human mortality is cancer. commercialized drugs successful based on bradykinin peptides derived from the snake venom(2). snake venom has been with various theraputic, anti viral, and antifungal activities(3). Therefore, the present review anticancer activity of the cobra venom componeuts agaist cancer(4).

Methods: Malaysian common cobras Malaysian is the venom snake species can be sepred into two families, three cobra species, name is Naja Naja, Naja sumatrana and Ophiophagus Hannah are the most common cobra(5). N.sumatrana is the most cobra of ten Elapid species. venom of mulaysian cobra Anticancer activity, antibacterial, anticonvulsant, and antithrombotic activities(6). Cobra venom consist of protein snake venom is a natural sour consist of proteins such as phospholipase A2, amino acid oxidase(8). The common and unique venom proteins from Naja Naja, Naja sumatrana, and Ophiophagus(9).

Results: Anticancer activity of cobra venom snake venom an important source of therapeutic and focusing on anticancer(10). cobra venom proteins have been isolated and their activity anticancer agents(11). almost of common cobra venom investigation into potential therapeutic, especially anticancer agents(12).

Conclusion: cancer is the most common problem world wide. anticancer agents naturally source specially animal venom for example snake venom,

scorpions and etc(13). protein is the most common in cancer therapy(14). cobra venom consist of protein and peptide(15). snake venom were widely studied. some venom peptides, for example cytotoxins are toxic natural understanding of the anticancer of the cobra venom(16). In conclusion, this review article anticancer activity of cobra venom componeuts against cancer(17).

Keywords: cobra venom, treatment cancer, snake venom, anticancer.

Antihistamines in insomnia : mechanism and side-effects (Review)

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Introduction: Insomnia is a complex disorder that affects a significant population of people and it involves many neurotransmitters including orexin, GABA, histamine, acetylcholine, dopamine, and Serotonin. Research has shown that people who don't have enough sleep suffer from depression, low quality of life, and physical dysfunction. The first line of therapy is cognitive-behavioral therapy for insomnia (CBT I). pharmacotherapy includes 4 classes of drugs (benzodiazepine receptor agonist, histamine receptor antagonist, orexin receptor agonist, and melatonin receptor agonist) named by SEDATIVE HYPNOTIC drugs. Between these drugs, antihistamines aren't FDA FDA-approved and to use them there have to be special circumstances. The antihistamines themselves are 4 types and only the first type, which can go through the blood-brain barrier (BBB) is used as a of the label drug for insomnia.

Methods: An authentic search was performed using PubMed and Scopus from 2000 to 2023. The search has been done with keywords including "insomnia," "first-generation antihistamines," "sedative hypnotics," "histamine," and "diphenhydramine". The Subjects used are, "Role of antihistamine in insomnia". "First generation antihistamines". "OTC drugs for insomnia". "treatment of insomnia".

Results: We reviewed 10 articles and in the end, we found out that first-generation antihistamines(H1 antagonists) like diphenhydramine are used as OTC drugs for insomnia which means that they don't have FDA proof. Using these drugs is not recommended especially in elderly people because of their side effects but we can use them in special circumstances. Their side effects are due to their anticholinergic effects on CNS and cause symptoms like nausea, diarrhea, and fatigue.

Conclusion: The majority of OTC drugs to aid sleep contain diphenhydramine, a nonselective histamine H1 -receptor antagonist that has significant affinity at other receptor subtypes leading to nonspecific side effects, including anticholinergic effects (sedation, dry mouth, blurred vision). Diphenhydramine has lack of clinical evidence supporting efficacy and safety. In the end, according to research although the first generation antihistamines

are OTC drugs for insomnia it's better to not use them unless the FDA-proven drugs wouldn't work or the insomnia was combined with an allergic disease.

Keywords: Keywords: insomnia, antihistamine, histamine, sleep, diphenhydramine, CNS

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Antimicrobial activity of copper nanoparticles derived by ajowan extract on Staphylococcus aureus and Escherichia coli (Research Paper)

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Introduction: In this study, the aqueous extract of Trachyspermum copticum seeds were used to synthesis copper nanoparticles and its antimicrobial activity was investigated.To identify the synthesized nanoparticles, different analyses, techniques and tools were used, including T.E.M imaging was performed and the size of the nanoparticles was determined. Other methods that were used is the XRD and Zeta potential methods, which according to the given graphs, each graph has alternating peaks, which shows the certainty of the synthesis.

Methods: The antimicrobial activity of copper nanoparticles synthesized using the micro dilution method was used for bacteria in Mueller Hinton culture medium, which was used e cording to the CLSI standard. In this method, eight wells started by 250 mg/ml and progressed half by half until well eight. In the extraction process, first about 19 grams of Trachyspermum copticum seeds were soaked in 190 ml of distilled water and storage in the refrigerator for 48 hours. After 48 hours 4 ml of the extract were added to one-tenth molar copper (II) oxide to a volume of 25 ml, and it was placed on a heater shaker at a temperature of 80oc for 1 hour, after adding the extract to the copper oxide solution changed from black to light brown.

Results: Synthesized nanoparticles showed activity against Staphylococcus auroras and Escherichia coli bacteria. Based on these data, copper nanoparticles derived by green method are the best choice for antimicrobial treatment.

Conclusion: The results showed that the aqueous extract of Trachyspermum copticum seeds acts as a rejuvenating and stabilizing agent. Synthesized copper nanoparticles showed activity against both Gram- positive (Staphylococcus aureus) and Gram-negative (Escherichia coli) bacteria.

Keywords: copper, Escherichia coli, Staphylococcus aureus, Trachyspermum copticum.

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Antimicrobial resistance of Escherichia coli isolates from outpatient urinary tract infections in women and male (Research Paper)

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Introduction: Escherichia coli is the main cause of community-acquired urinary tract infections (UTIs). The aims of the present study were to examine the susceptibility profile of E. coli causing UTIs and to identify factors associated with antimicrobial resistance.

Methods: A cross-sectional study was conducted in Arak City, Iran, between 2022and 2023. Patients referred to Laboratory Bozorgmehr and diagnosed with UTI caused by E. coli were enrolled in the study. Susceptibility testing to commonly used antimicrobial agents was performed by the disk diffusion method. Relevant data were abstracted, and analysis was performed to identify factors associated with antimicrobial resistance. A total of 91 E. coli isolates from 1300clinical urine samples were collected.

Results: Overall AMR rates to the commonly used antibiotics nitrofurantoin, Amikacin ,Ceftriaxone,Ceftazidime,Ciprofloxacin,Trimethoprimsulfamethoxazole and Imipeneme,were 3.19%, 4.21% ,23.07%,20.87% ,39.56%,46.1%, 27.47%respectively. The highest overall resistance rates were determined for ampicillin (90.2%), amoxicillin-clavulanic acid (81.1%), The rate of extended-spectrum β-lactamase (ESBL) production was 14.2%.

Conclusion: This survey says the cause of high resistant Escherichia coli strainsto Ampicillin antibiotics and amoxicillin-clavulanic are too take this antibiotics. Then, preventing from use of un necessary antibiotics and take care of production new and drastic antibiotics will be recommend.

Keywords: Outpatient UTI Escherichia coli Antimicrobial resistance

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Apigenin Impact on Breast Cancer: A Mechanistic Study Based on Network Pharmacology (Research Paper)

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Introduction: Based on the WHO report, breast cancer (BC) was the most commonly diagnosed cancer among women in 2020, which counted for 1 in every six deaths caused by cancer in women. Humanity has a long history of using plant-derived compounds as medicine, especially for cancer treatment. Flavonoids are among the most important natural compounds with various pharmacological properties, including their significant anti-cancer activities. Apigenin, also known as 4′,5,7-trihydroxyflavone, is a member of the Flavonoids family commonly found in various food plants and herbs such as parsley, onions, oranges, chamomile, and oregano.

Methods: In this study, we used Pubchem, Binding DB, SwissTargetPrediction, Similarity Ensemble Approach (SEA), TargetNet, GeneCards, Way2Drug, DAVID, and DisGeNET databases to identify the BC-related Apigenin targets. Furthermore, we used the STRING database to explore the protein-protein interactions of BC-related proteins when exposed to Apigenin and the gene ontology of these proteins. Cytoscape 3.9.1 illustrate the data network. Autodock Vina 4.2 and Discovery Studio 4.5 conducted molecular docking.

Results: The gene ontology data revealed that enzyme binding, macromolecular complex, and positive regulation of transcription from RNA polymerase II promoter are the most probable processes under the influence of Apigenin. Based on the network pharmacology, AKT1 and EGFR

(Epidermal Growth Factor Receptor) are the most influential targets in relation to BC. The affinity of Apigenin towards AKT1 and SHBG was identical, with releasing the energy of -7.6 Kcal/mol for both. In addition, estimations demonstrate that AKT1 and SHBG are more effective against the MCF7 cell line. Several studies have shown that Apigenin exhibits potent anti-BC activities through the induction of apoptosis and cell proliferation arrest. One study revealed that the inhibition of Akt by Apigenin causes the downregulation of MMP-9, a key promoter for metastasis in cancer cells. EGFR plays an essential role in regulating and maintaining BC cell characteristics such as metastasis, proliferation, and invasion. Apigenin has been proven to decrease the expression of EGFR. These studies validate our finding on Apigenin's activities against BC.

Conclusion: In conclusion, based on the results of recent studies and ours, Apigenin shows great potential as an active agent against several breast cancer cell lines with multiple pathways causing apoptosis and cell cycle arrest.

Keywords: Apigenin, Breast Cancer, Network Pharmacology, Molecular Docking

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Apoptosis in the fight against invasive cancer cells with the help of herbal bioactives (Review)

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Introduction: Considering the prevalence of cancer in most countries of the world, A variety of treatment methods have been widely used for cancer. Cancer cells disrupt the regulation of the cell cycle by their abnormal proliferation and growth and sometimes metastasize. To reduce the lethal effect of these invasive cells, it is necessary to seek recovery and treatment as soon as possible. One of the new treatment methods for cancer is Car T-cell therapy. This method can provide chimeric antigen receptors on T cells in the blood that diagnose cancerous tumors. It sometimes causes death. Other methods used such as Chemotherapy, hormone therapy, and cell therapy have many side effects for cancer patients. For this reason, to improve the condition of patients who have a hard time tolerating the side effects of chemical drugs, they use natural drugs such as herbal extracts that are obtained according to various laboratory processes. Plants contain several classes of phytochemicals, including tannins, saponins, phenols, flavonoids, and alkaloids. These substances can have antioxidant, anticarcinogenic, antimutagenic, cytotoxic, anti-inflammatory, antibacterial, and antiviral properties.

Methods: Data for this review article were collected from 40 published articles in Full-text forms (original, review, and case reports/series studies) obtained from Science Direct, PubMed, Elsevier, and Google Scholar from 2019 to April 2023. Data and articles that were far from the desired sub-topic were removed.

Results: Herbal medicines in cancer treatment should act in such a way that they affect DNA synthesis or cell mitosis. In this way, they prevent or stop the formation of DNA and the start of mitosis in the cell cycle to prevent the growth and proliferation of malignant and mutated cells and cause them to decrease. Also, herbal medicines cause apoptosis (programmed cell death) which is an essential physiological process in the cell.

Conclusion: Bioactive molecules play an essential role in the apoptosis of cancer cells. Antioxidants that are produced naturally in the human body, and even antioxidants that we get as supplements and nutrition, play an important role in the health of the human body and inhibit cancerous tumors. We can use all the parts of some medicinal plants such as turmeric, garlic, aloe vera, and rosemary, as well as the oil and extract obtained from them, as well as the ethanol obtained from the seeds of some plants, for treatment. we hope to eradicate such diseases with herbal medicines.

Keywords: cancer, herbal medicines, bioactive, cytotoxic

Apoptosis induction in human hepatoma by trans- Anethole via activation of apoptotic pathways (Review)

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Introduction: Liver cancer is the fifth most common type of cancer and it is the second most common cause of cancer-related mortality globally, with an estimated 746,000 deaths in 2012. The incidence of liver cancer and mortality shows a stable increase worldwide. An estimated incidence of primary liver cancer ranges from 600,000 to 800,000 annually, accounting for 5.6% of all human cancers and projected cases of about a million by 2030 . Liver cancer consists of a heterogeneous group of malignant tumors with varied histological characteristics and unfavourable prognoses. The major hepatocellular neoplasms include hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA), hepatoblastoma, hepatocellular adenoma, and the pediatric neoplasm. HCC is the most common and iCCA is the second most common primary liver cancer.There are many naturally occurring compounds of plant origin which are known to exert protective effects against the genotoxicity and carcinogenicity of the environment. Dietary intake of such chemopreventive compounds has been suggested as an effective strategy for minimizing the deleterious effects of genotoxins and carcinogens. Trans-anethole is a constituent of the volatile component of more than 20 spices. It is the major volatile component in sweet and bitter fennel and anise. Trans-anethole is used as a flavouring substance in baked goods, candy, ice cream, chewing gum and alcoholic beverages. Enzyme induction studies in mice and/or rats suggest that trans-anethole and eugenol are effective inducers of detoxifying enzymes (Phase II enzymes)

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Trans-anethole is a valuable compound derived from star anise widely used by ethnic tribals to manage numerous human diseases. In this study, antiproliferative activities of trans-Anethole towards human liver cancer (HepG2), cervical cancer (HeLa) and breast cancer (MCF-7) cells were explored. Trans-anethole showed free radical scavenging potential as assessed by DNA nicking assay. Trans-anethole exhibited strong antiproliferative potential towards HepG2 cells compared to other cell lines. trans-Anethole strongly induced apoptosis in HepG2 cells by significantly

upregulating the protein expressions of p53, Caspase-3 and Caspase-9 were assessed by western blotting analysis which highlighted the apoptosis-inducing capacity of trans-Anethole against HepG2 cells. Rt-qPCR analysis revealed that trans- Anethole upregulated p53, caspase 3 and 9 in comparison to untreated HepG2 cancer cells. Moreover, trans-Anethole provoked the generation of ROS and disruption of MMP.

Conclusion: Our research suggests that trans-Anethole may have a significant anticancer therapeutic potential for treating liver cancer. The results revealed that trans- Anethole significantly inhibited the proliferation of HepG2 cells and induced apoptosis via ROS generation and disruption of MMP. Further, it induced the apoptotic process by modulating the caspase 3, caspase 9 and p53 levels.

Keywords: Apoptosis, hepatoma, trans- Anethole, pathways

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Apoptotic Effects of C-82 and Naringenin on Menstrual Blood-derived Mesenchymal Stem Cells of Endometriosis Patients (Research Paper)

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Introduction: One of the leading causes of endometriosis - a chronic estrogen-dependent disease associated with pelvic pain and infertility- is the return of menstrual blood flow into the pelvic cavity and the establishment of menstrual blood mesenchymal stem cells (MenSCs) in areas outside the uterine cavity. MenSCs from endometriosis patients (E-MenSCs) and healthy women have been shown to vary, particularly in terms of surface markers and gene expression, which may suggest the involvement of these cells in the development, expansion, and maintenance of ectopic lesions. The purpose of this study is to investigate the effect of small molecule C-82 and naringenin as inhibitors of involving pathways on endometriosis to modulate their gene expression and functional pattern.

Methods: The menstrual blood samples were obtained from endometriosis patients through the day 2-3 of menstruation cycle. Based on density gradient method, stromal cells were isolated from the samples by means of Ficoll-Paque and were cultivated in DMEM with 10% FBS and 1% penicillin/streptomycin and incubated at 37°C, 5% CO2, and 95% humidity.In the 3rd passage, E-MenSCs were treated with C-82 and naringenin. Then, cell behavior was studied using annexin V/PI assay. After reaching 70% confluence in passage 3, the cells were seeded in proper dishes for 24 hours. Then, the small molecule group and the naringenin group were cultured with fresh medium containing 2 µM small molecule C-82 (Sigma-Aldrich, Lyon, France) and 100 µM naringenin (Sigma-Aldrich), respectively. The same

amount of C-82 and naringenin for SM and Nr groups, were used simultaneously for treating SM/Nr group. The control group received no treatment. The time of treatment for all groups was 72 hours.

Results: Annexin V/PI assay The effects of applied treatments (C-82 and Naringenin, alone or together) on the apoptosis of E-MenSCs were assessed through flow cytometry with annexin V and PI detection kit (Fig.2). As expected , the obtained data showed a significant increase in early apoptosis of Combination treatment of Nr with SM co-treated SM/Nr group in comparison with untreated E-MenSCs ($p= 0.0232$) . SM group ($p= 0.0293$), while although C-82 and Naringenin alone increased the early apoptosis percentage in treated cells but they did not elevate it in a statistical significant way ($p= 0.9991$ and $p= 0.2141$, respectively). However, it was demonstrated that none of the applying treatments could exert a significant change in the percentage of the late and total apoptosis ($p>0.05$) (Fig.2). BAX/BCL2 gene expression Next, we evaluated apoptotic related genes, that showed C-82 and combination of C-82/Naringenin significantly increase expression of BAX (proapoptotic gene) and BCL-2 (antiapoptotic gene) as compared with control group ($p= 0.00$), while no significant change was observed in Nr group ($p>0.05$). So, when the BAX/ BCL2 ratio was assessed, none of the treated group were different from the untreated E-MenSCs ($p>0.05$) (Fig.3).

Conclusion: In the present study, increased early apoptosis was observed in E-MenSCs after treatment. We observed that small molecule C-82 together with naringenin can promote apoptosis in E-MenSCs. These results are significant because they clarify the function of C-82 and naringenin in endometriosis. Further research is needed to analyze the precise effects of small molecule C-82 and naringenin on endometriosis E-MenSCs.

Keywords: endometriosis, mesenchymal stem cells, menstrual blood, small molecule C-82, naringenin

Application of 3D organoid for early diagnosis prognosis, and therapeutic approaches of oral cancer (Review)

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Introduction: Oral cancers are the sixteenth most common cancer worldwide, with 90% comprising oral squamous cell carcinoma (OSCC), affecting more than 300,000 individuals annually. Alcohol drinking, tobacco consumption, and human papillomavirus (HPV) infection are the main high-risk factors for oral cancers. Conventional treatments include chemotherapy, radiotherapy, and surgery that have not significantly reduced the high morbidity rate. Late diagnosis in the end stage of OSCC and the absence of a definitive biomarker for early diagnosis through clinical examination and histopathological analysis remain poor prognoses.

Methods: Recent studies revealed that biological fluids, including blood, urine, saliva, etc., have the potential for early diagnosis. Some benefits of the biofluid assessment include accessible sample collection, noninvasive sampling, and economical and valid outcomes. In addition to the late diagnosis, selecting appropriate individual therapeutic approaches is another challenge in oral cancer patient management. Since oral cancers, specifically OSCCs, are heterogenous, we need reliable individualized therapy that predicts clinical responses. Personalized medicine or precision medicine has opened a new avenue for therapeutic approaches based on the unique genetic profiles of individuals following the variation. This genomic signature causes different responses to the therapy to apply appropriate drugs with minimum side effects. The advanced technology of high-throughput analysis, next-generation sequencing (NGS), microarray, transcriptomics, and proteomics promote the knowledge of specific variants that can affect therapeutic approaches.

Results: Organoid technology provides this opportunity for preclinical prediction and response to treatment before being applied to patients. In recent years, three-dimensional (3D) culture technologies known as "mini-

organ" have been rapidly developed, which is a three-dimensional (3D) structure that mimics morphological, functional, and genetic characteristics of the target tissue of origin in a specific scaffold. Tumor organoids derived from patients (PDO) can be applied for drug screening and biomarker detection. Organoid technology is suitable for studying heterogeneous tumors such as oral cancers. Human organoid models are established from two types of stem cells, including pluripotent stem cells (PSCs) and adult stem cells (ASC), with the self-renewal ability and potential for multi-differentiation. Then, 3D organoids can be applied for regenerative medicine, tissue engineering, and disease modelling. Single-cell high throughput analysis by circulating tumor cells (CTCs) and genetic manipulation by gene editing technology are the other critical applications of organoids for oral cancer.

Conclusion: Organoids allow us this opportunity to evaluate the pathogenesis of cancer, tumor cell behaviour in a mimic environment, and drug screening in a living biobank due to personalized medicine.

Keywords: Organoid, Precision medicine, Oral cancer, Early diagnosis, Oral squamous cell carcinoma

Application of Antibody-Conjugated Magnetic Nanoparticle in Drug Delivery: A Systematic Review (Review)

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5.

Introduction: Magnetic nanoparticles (MNPs) have gained considerable attention as drug delivery vehicles due to their unique magnetic properties and high surface area. Antibody-conjugated MNPs have been developed as a targeted drug delivery system, enabling the specific delivery of drugs to target cells or tissues. This systematic review aims to evaluate the current knowledge on the application of antibody-conjugated MNPs in drug delivery, including their synthesis, characterization, and efficacy in vitro and in vivo.

Methods: A comprehensive literature search was conducted using PubMed database. The search strategy included the keywords ((delivery[Title/Abstract])) AND (antibody[Title/Abstract]) AND ((magnetic[Title/Abstract]) OR (iron[Title/Abstract]))." Only studies published between 2020 and 2022 were included in the review.

Results: A total of 84 studies were included in this review. The studies investigated the synthesis, characterization, and efficacy of antibody-conjugated MNPs in drug delivery for various diseases, including cancer, cardiovascular diseases, and infectious diseases. The results showed that antibody-conjugated MNPs can enhance the specificity and efficacy of drug delivery by targeting specific cells or tissues. Moreover, the physicochemical properties of MNPs, such as size, shape, and surface charge, can affect their efficacy in drug delivery. Several in vitro and in vivo studies have

demonstrated the potential of antibody-conjugated MNPs in targeted drug delivery, with promising results.

Conclusion: The findings of this systematic review suggest that antibody-conjugated MNPs have potential as a targeted drug delivery system for various diseases. The physicochemical properties of MNPs, as well as the choice of antibody and drug, can affect the efficacy of drug delivery. However, further research is needed to optimize the synthesis and characterization of antibody-conjugated MNPs, to evaluate their safety and efficacy in human clinical trials, and to explore their potential combination with other drug delivery systems.

Keywords: Drug Delivery, Iron, Magnetic, Nanoparticle, Antibody

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Application of Artificial Intelligence in Predicting Gastric Cancer-associated Single Nucleotide Polymorphisms (SNPs): A Comprehensive Review (Review)

Amin Enayati,[1,*]

1.

Introduction: Gastric cancer, a leading cause of cancer-related death globally, is driven by a combination of environmental, genetic, and epigenetic factors. Single nucleotide polymorphisms (SNPs) have emerged as critical biomarkers for understanding individual susceptibility to this malignancy. The colossal amounts of genomic data necessitate advanced computational tools to discern patterns and predict SNPs that significantly impact the development of gastric cancer. This review delves into the innovative integration of artificial intelligence (AI) methodologies in forecasting gastric cancer-associated SNPs.

Methods: Literature databases were thoroughly scanned to consolidate research that utilized AI-driven algorithms, including but not limited to machine learning and deep learning, for SNP prediction related to gastric cancer. The selected studies were evaluated based on the AI model used, dataset size, SNP identification process, validation strategies, and prediction accuracy.

Results: AI has revolutionized the identification of gastric cancer-associated SNPs, outperforming traditional statistical methods in terms of speed and accuracy. Several studies have employed machine learning models, including support vector machines, random forests, and neural networks, showing prediction accuracies that often surpass 90%. Deep learning methodologies, though in their infancy in this domain, have showcased potential, especially convolutional neural networks (CNN) and recurrent neural networks (RNN). The integration of feature selection methods with AI models has further improved prediction accuracy by identifying pertinent genomic features and reducing computational complexity. While most studies utilize public genomic databases, the emergence of large-scale multi-omics datasets has empowered models to consider gene-gene and gene-environment interactions, providing a holistic view of SNP-gastric cancer associations. Discussion: Despite the advancements, challenges remain. Balancing the trade-off between model complexity and interpretability, managing imbalanced datasets, and integrating diverse data types are key areas for improvement. Moreover, the translation of AI-predicted SNPs into clinical settings

necessitates rigorous validation and a deeper understanding of the functional implications of these SNPs.

Conclusion: AI, with its capacity to process and analyze vast genomic datasets, has demonstrated remarkable potential in predicting SNPs linked to gastric cancer development. Its continued refinement and integration with multi-omics data are set to offer unprecedented insights into the genetic underpinnings of gastric cancer, thereby advancing personalized medicine and therapeutic strategies.

Keywords: Gastric cancer , Artificial Intelligence, Single Nucleotide Polymorphisms (SNPs)

Application of Biosensors in the Analysis of Biochemical Markers (Review)

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Introduction: Biosensors are biological molecules that have the ability to accurately detect and measure biological molecules and by producing a signal, announces information about the current situation. Recent technological advances have led to the development of this technology and accelerating the process of diagnosing and treating diseases, identifying biomarkers, cancer cells, as well as tracking the response of the patient's body to treatment and direct measurement of biochemical activities in biological samples before and after drug administration. The purpose of this study is to investigate the progress and application of biosensors in order to identify and detect effective biochemical factors in the diagnosis of diseases and their treatment.

Methods: In this review study with library methods, relevant articles from databases were studied in order to investigate the application and use of biosensors in the detection of biological molecules, acceleration of the treatment process and analysis of the healing process of diseases.

Results: Studies have shown that the use of biosensors for the analysis of biochemical markers in patient samples, due to the accurate detection of enzyme molecules and the evaluation of analytes, provides an opportunity for early diagnosis and treatment of diseases, the presence or absence of biomarkers. It has been found that biosensors play an important role in the detection of specific biomolecules, which will be very useful for new assays of extracellular exosomes, blood biopsies and body fluids of patients with the help of this technology in the field of oncology. Today, with the increase in sensitivity of immunobiochips and the detection of exosomal RNAs, cancer diagnosis is also done, and biosensors based on protein receptors are being investigated. Modern nanotechnology, innovative enzyme engineering, sophisticated sequencing program-based designs, and precise in vivo/in vitro applications for DNA-based biosensors have all facilitated their use but

accurate time measurement of metabolite biomarkers still requires the development of in vivo sensors.

Conclusion: Considering the functional characteristics of biosensors such as stability, sensitivity and high efficiency in the pharmaceutical and clinical field, its small size and its role in medical applications compared to conventional techniques, its use in early clinical diagnosis with regard to the complex biomarkers of organisms and environmental factors. And genetics is still a big challenge, but its use has led to a new approach in medical science that, with further progress, can increase the quality of life of patients.

Keywords: Biosensor, Biochemical Markers, Diagnosis, Treatment, Enzyme Engineering

Application of body fluid biomarkers as a reliable strategy for early diagnosis, prognosis, and therapeutic approaches to oral cancer (Review)

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2.

Introduction: Introduction: Oral squamous cell carcinoma (OSCC) comprises more than 90% of oral cavity cancer with a high mortality rate. The five-year survival rate for OSCC is around 85% in early diagnosis, but the patients are referred when they develop advanced stage, and the survival rate remains as low as 15%–50%. Thus, early diagnosis is pivotal to promoting survival rate and prognosis for OSCC patients. Leukoplakia, erythroplakia, oral lichen planus, and oral submucous fibrosis are potentially oral malignant disorders (OPMDs) that can transform into OSCC. According to the type of lesion, the malignant transformation rate may range from 0% to 20% in 1–30 years. Thus, clinical examination, besides oral cancer screening by reliable biomarkers, is critical in high-risk groups for early diagnosis, prognosis, and application of therapeutic approaches.

Methods: Literature review: Recent studies highlighted that body fluids such as saliva, serum, plasma, and urine can be applied for disease monitoring. The body fluids contain reliable biomarker profiles during the tumorigenesis process that demonstrate early diagnosis, recurrence, survival, the beginning stages of invasion, metastasis, and angiogenesis process, and pharmacological response to therapeutic intervention.

Results: There are many benefits of using saliva as a biofluid: easily accessible, inexpensive, noninvasive collection, safe to handle in comparison to the blood, the possibility of greater volume for assessment, and repeated sampling for monitoring many times, easy to store as it does not clot, the potential of self-collection by patient removes direct interaction with investigators, thus decreasing the risk of infections, and applicable for mass screening of large population. In this way, the saliva, known as a "mirror of the body", can reflect the physiological and pathological situation of the body. "Salivaomics" constituents of saliva that comprise proteome, transcriptome, metabolome, and microbiome profile signature. This technology allows us to detection of circulating tumor cells (CTCs) and fragments of tumor DNA in

saliva for early detection of various cancers. CTCs carry on unique genomic, transcriptomic, and epigenomic signatures of tumor nature.

Conclusion: Conclusion: Body Fluid biomarkers, especially saliva, can be a reliable strategy for early diagnosis, prognosis, and therapeutic approaches in oral cancer. In addition, detecting and diagnosing malignant lesions can be considered for human immunodeficiency virus, heart disease, and autoimmune diseases.

Keywords: Oral squamous cell carcinoma,Oral cancer,Biomarkers, Body fluids,Saliva,Circulating tumor cells.

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Application of microRNAs as potential biomarker for early diagnosis, prognosis, and therapeutic approaches of oral cancer (Review)

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Introduction: Background: Oral cancer is known as the sixteenth most common cancer around the world, and oral squamous cell carcinoma (OSCC) comprises 90% of them with more frequency in South-Asian countries. The most commonly discovered risk factors are tobacco and alcohol consumption, and human papillomavirus (HPV) infection. The current therapeutic approaches are chemotherapy, radiotherapy, chemo/radiotherapy, and surgery. Although many studies have been developed to provide definitive biomarkers for early diagnosis, prognosis, and therapy, the five-year survival rate remains poor at 50%. In this way, it is essential to provide novel diagnostic tools and targeted therapies.

Methods: Literature review: The genes involved in molecular pathways of the tumorigenesis process are regulated by some non-coding RNAs such as microRNAs (miRNAs or miRs). miRNAs are small-length sequences (21-23nt) that regulate gene expression at the post-transcriptional level by degrading or suppressing target messenger RNAs (mRNA) according to the partial complementary base pairing sites. miRNAs commonly bind to the 3' untranslated region (3' UTR) of target mRNA by degrading them or rarely attaching to the 5' UTR to suppress promoter activation. Based on previous studies, deregulation of miRNAs affects downstream gene expression and plays a role in the pathological processes of oral cancer. The miRNAs can repress tumor suppressor gene expression by the oncogenic role that is named onco-miRs or inhibit the expression of oncogenic genes. This idea of application of them as potential biomarkers was manifested for early diagnosis, prognosis, and the development of novel therapeutic approaches. In addition, miRNAs can be involved in epigenetic modification by binding to the histones during methylation. One of the key findings in recent studies is the evaluation of miRNAs in body fluid in mentioned strategies for oral cavity cancers.

Results: The body fluid contains a signature profile of markers that change their expression during the tumorigenesis process, metastasis, and invasion. The biofluid collection is non-invasive, available, economical, safe, and valid.

Micro-RNAs (miRNAs) are one of the critical cell-free nucleic acid elements in body fluids such as saliva, serum, plasma, and urine. Despite the potential roles of circulating miRNAs, challenges remain related to the exact regulation of mentioned miRNAs before using them in targeted therapy. Since one miRNA can bind to multiple mRNA targets, and one mRNA can attach by different miRNAs, discovering a definitive miRNA biomarker is the main challenge. Evaluating potential biofluid markers in the clinical setting would allow us for early diagnosis, prediction of treatment response, improvement in treatment candidates, and disease monitoring for early detection of tumor recurrence.

Conclusion: Conclusion: A panel of candidate distinct miRNAs may indicate clinicopathological features, the result of personalized treatment, and provide new signature profiles of oral cancer. miRNA signatures can be applied as potential biomarkers for early oral cancer diagnosis, and prognosis and as novel molecular therapies in oral cancer.

Keywords: Keywords: miRNAs, Oral cancer, Biomarkers, Epigenetics, Early diagnosis

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Application of nanobiomaterials to improve angiogenesis in tissue engineering (Review)

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Introduction: Angiogenesis, a crucial step in the wound healing process, provides sufficient oxygen and nutrients to the wound site. The use of nanostructures has become an effective way to regulate the biological functions of cells. Biological nanomaterials have attracted a lot of attention in biomedical applications due to their unique structure and photoelectric and catalytic properties. Nanobiomaterials, such as nanoparticles and nanofibers, can be engineered to release growth factors or other bioactive molecules that promote angiogenesis. Nanomaterials not only act as carriers that effectively deliver factors such as angiogenesis-related proteins and mRNA, but also mimic the nanotopological structure of the primary ECM of blood vessels and stimulate gene expression of angiogenic effects that facilitate angiogenesis.

Methods: A document search was conducted on the Scopus database, Google Scholar and PubMed database of studies published from January 2015 to September 2023 with English keywords, including gene editing, nanobiomaterials, angiogenesis and tissue engineering. A combined Hunt of keywords was done using Boolean drivers AND and OR. Data analysis was done qualitatively.

Results: Among the nanomaterials with angiogenic properties include: Gold, Cu2S, HA, TCP, Bioactive glass nanoparticle/nanofiber, Zinc oxide nanoflowers/ nanoparticles, Terbium hydroxide rods/ spheres, Neodymium, TiO2 ,are effective in regenerating hard and soft tissues (mainly bone and

skin, respectively). It is possible to increase the efficiency of nanofibrous scaffolds in order to improve tissue repair and regeneration in different ways, such as: simultaneous delivery of angiogenic growth factors such as: PDGF, (TGF-β), angiogenin and other bioactive molecules (bioactive glass), use of small angiogenic molecules such as angiogenin and phytochemicals (such as curcumin), surface functionalization of nanofibrous scaffolds with angiogenic bioactive molecules, addition of inorganic elements (such as cerium and europium), highly controlled doping of angiogenic elements to the structure of bioceramics (eg, calcium phosphate and glass bioactives), implantation of various somatic and stem cells such as endothelial cells (ECs) and mesenchymal stem cells (MSCs). In general, the use of some natural and synthetic polymers that have inherent angiogenic properties for example, hyaluronic acid, collagen, elastin, PLA, PCL, PLCL, hyaluronic acid and their composites leads to an increase in the expression of angiogenic growth factors and cytokines, including VEGF -D, matrix metalloproteinase-2 (MMP2), matrix metalloproteinase-3 (MMP3) and matrix metalloproteinase 19 (MMP19).

Conclusion: Therefore, the electrospun nanofibers benefit from the high loading efficiency of therapeutic agents due to the high surface area to volume ratio compared to other conventional nanoscale delivery vehicles such as liposomes, polymeric micelles, and complexes. In addition, the tunable properties of the polymer matrix (eg, porosity, diameter, and morphology) allow the incorporation of various drugs into the electrospun scaffolds, thus leading to effective local delivery of drugs to the target tissue.

Keywords: Nanobiomaterials, Angiogenesis, Tissue engineering

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Application of nanotechnology in cancer therapy (Review)

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Introduction: Despite the significant advancements in conventional treatment modalities such as chemotherapy and radiation, the field of cancer therapy still faces certain limitations that restrict its ideal effectiveness. Current cancer therapies sometimes face several problems. These challenges include the nonspecific systemic distribution of anticancer drugs, insufficient drug concentrations reaching the tumor site, severe cytotoxicity, a lack of ability to monitor therapeutic responses, and the emergence of multiple drug resistances. In recent years, there has been significant focus directed towards the utilization of nanotechnology in the field of cancer therapy. It offers a distinctive approach and comprehensive technology against cancer through early detection, prevention, prediction, medicine, and personalized therapy. The primary areas of research that prioritize the utilization of nanotechnology are target-specific medication therapy and early diagnosis approaches for diseases. Numerous research studies have employed nanoparticles in the field of cancer immunotherapy due to their various advantages over conventional approaches to cancer treatment. Initially, nanoparticles provide affirmative cover for susceptible proteins or antigens, which can be deactivated or degraded with enzymes in complex physiological conditions. Furthermore, by manipulating formulations, it is possible to manufacture nanoparticles that may effectively encapsulate specific cargo with a high degree of efficiency. This review explores cancer nanotechnology's approaches to improving the effectiveness of cancer therapy.

Methods: A comprehensive search was conducted over nine databases to discover published articles related to cancer therapy using nanotechnology from January 2000 to January 2023. A total of 5,000 studies were funded based on the keywords searched, such as Nanotechnology, Cancer, Chemotherapy, and Immunotherapy. 300 went for full reading texts. 100 relevant articles with complete abstracts were included in the study.

Results: Nanoparticles have been used a lot in recent preclinical studies as ways to deliver immune-stimulating chemicals and tumor antigens to DCs and other APCs in a controlled and steady way. Nanoparticles can also serve as carriers for passing around immunosuppressive impulses and environments resulting from tumors by putting ICBs along with other small compounds on them. Positive results from these studies show that cancer immunotherapy involving nanoparticles may lead to effective responses from T-cells and improve anti-tumor effects in both ways. In addition, phototherapy and chemotherapy in combination with nanoparticle delivery systems can enhance immunotherapy against cancer. One advantage associated with the utilization of nonviral vectors is the ability to administer them repeatedly at a low cost while also minimizing immunological reactions due to their non-toxic nature. Liposome-mediated cationic polymers and nanoparticles are the nonviral vectors that are most commonly used. The evaluation of nanoparticles as prospective nonviral gene vectors relies on several crucial factors, including morphology such as shape, size, charge density, and colloidal stability. The combination of various immune checkpoint inhibitors with nanoparticles is a potent approach for significantly enhancing the efficacy of anticancer responses. Thankfully, nanoparticles are versatile carriers that can be used in conjunction with treatments like photothermal therapy and chemotherapy to contain not only antibodies but also vaccinations or medications.

Conclusion: During the past few years, nanotechnology has shown a substantial increase in its applications in the area of cancer nanotechnology. With nanoparticles, it is possible to develop and adjust features that are not possible with other therapeutic drugs. As the next generation of cancer therapeutics, they appear to have a promising future. Despite its multidisciplinary nature, nanotechnology exhibits the potential to yield significant technological advancements. It is progressing rapidly in its transition from theoretical constructs to practical applications.

Keywords: nanotechnology, cancer, chemotherapy, immunotherapy

Application of salivaomics for early diagnosis, prognosis, and therapeutic approaches of oral cavity cancer by molecular biomarkers (Review)

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Introduction: Oral cavity cancer is the sixteenth most common cancer worldwide, with oral squamous cell carcinoma (OSCC) comprising more than 90% of it. There are no definitive early diagnosis biomarkers for oral cancer screening because of the heterogeneous nature of oral cancer. The five-year survival rate for OSCC remains low at 15%–50% Since the patients report when they develop advanced stage; however, early diagnosis can promote it at around 85%. In this way, early detection plays a critical role in improving survival rates and prognosis for patients. Saliva, the most non-invasively collected body fluid, is evaluated for biomarkers, specifically in liquid biopsy, that can provide a considerable platform number of molecules correlated to oral cavity cancer. Human saliva provides whole-body images and is introduced as a “mirror of the body's health.” Evaluation of biofluid markers can be applied for early diagnosis, prognosis, and therapeutic approaches to oral cancer.

Methods: Although biopsy is known as the ultimate gold standard for diagnosing oral cancer, advanced techniques have been developed to predict the oral tumorigenesis process. Due to the development of the salivary proteome, transcriptome, metabolome, and microbiome as valuable diagnostics indices, saliva can be applied for personalized or precision medicine. Non-coding RNAs, microRNAs, mRNAs, circulating tumor cells, exosomes, extracellular vesicles, antigens, and other proteins can be assessed from saliva. These biological molecules can play a pivotal role in the etiopathogenesis of oral cancer and can applied in early diagnosis of oral cavity cancer. Hence, this technology has been applied as sensitive, noninvasive, cost-effective, and patient-friendly for assessing biomarkers.

Results: In addition, salivaomics was applied to diagnose colon cancer, type II diabetes, breast cancer, renal diseases, and cardiovascular diseases. The profile signature of genomic, transcriptomic, epigenomic, etc., can be assessed by single-cell analysis due to salivaomics. The protein, RNA, and DNA molecules can act as oncogenes to promote tumorigenesis or tumor suppressors to inhibit tumor development based on their targets. Their

dysregulation can affect cell growth, apoptosis, differentiation, invasion, metastasis, inflammation, and immunity.

Conclusion: Salivaomics can be applied as a reliable method for screening and monitoring oral cancer patients by saliva molecule biomarkers. This method can discover novel biomarkers and be applied for future early diagnosis, prognosis, and therapeutic approaches.

Keywords: Mouth Neoplasms, salivaomics, Biomarkers, Saliva

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Application of Triboelectric Nanogenerators in Regenerative Medicine (Review)

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Introduction: Regenerative medicine has created many hopes for the treatment of many organ defects and diseases. On the other hand, the role of electrical stimulation in improving the function of stem cells in regenerative medicine has been well proven. Therefore, the increasing need to provide electrical energy without the common challenges related to batteries such as heat generation and cell destruction has led to the expansion of research towards the use of nanogenerators in modern medical applications and especially in regeneration.

Methods: In this review, PubMed, ISI Web of Science, Google scholar and SCOPUS databases were searched for studies published up to September 2023 related to “Application of Triboelectric Nanogenerators in Regenerative Medicine” were addressed.

Results: The review of studies showed that triboelectric nanogenerators with electrical energy supply from mechanical movements and advantages such as lightness, flexibility, as well as reduced toxicity and no need for re-surgery can be considered as one of the most important advantages of using triboelectric nanogenerators in regenerative medicine. Also, the examination of the results showed that the electrical stimulation from the nanogenerator can help in wound healing, bone and nerve regeneration.

Conclusion: The use of nanogenerators in preparing scaffolds can create new horizons in tissue engineering and regenerative medicine.

Keywords: Electrical Stimulation, Triboelectric, Nanogenerators, Regenerative Medicine.

applicaton of spirulina in beauty and cosmetics (Review)

shokouheskandarinazhad,[1,*]

1.

Introduction: For several years, the word spirulina has been well known, especially in the world of food and feed. This cyanobacterium consists of "B" group vitamins, iron and protein, which makes it a food supplement or another raw material in avant-garde restaurant dishes.Its popularity has been such that it is being called a new "superfood" due to its richness in nutrients such as calcium, potassium, magnesium, niacin, and those already named. In addition, it has also been used as a treatment for weight loss and obesity, treatment of diabetes or high cholesterol, although this has been scientifically rejected by the World Health Organization (WHO).

Methods: we use microalrea_spirulina plantensis_water_zarrouks medium calture_NAHCO3_HEATER_PLATES for medium calture_lLED lightes_sonication_labratory instrumentes

Results: As reviewed in this article, the commercial algae spirulina is a potential biological component For the development of effective and safe cosmetics. In recent years, the benefits of skin care Algae products are investigated by academic researchers and various commercial companies in this active field has taken. As reviewed in this article, the commercial algae spirulina is a potential biological component For the development of effective and safe cosmetics. In recent years, the benefits of skin care Algae products are investigated by academic researchers and various commercial companies in this active field has taken.

Conclusion: Therefore, these products may be used topically as a booster and preventative. And in sunscreen and anti-wrinkle creams for , to treat skin disorders and achieve wound healing benefits Despite recent developments, this issue needs to be addressed Venice should be studied in more depth than cosmetic products based on Improve spirulina algae in the long term. Spirulina algae may exhibit antimicrobial activity in the treatment of microbial and bacterial skin diseases. As a result, it is in both cosmetic and skin fields More research is needed on the antimicrobial activity of algae in the skin. Therefore: the use of spirulina algae in cosmetics: Currently, various products based on materials derived from the sea have been marketed for different purposes. These substances have various properties, including anti-aging properties, skin whitening and moisturizing, food supplements, treatment of

skin and hair disorders, and ultraviolet rays filter. Green Sea provides products based on seaweed, which includes spirulina capsules and edible capsules, and these products will increase over time.

Keywords:
spirulina_spirulinaplantensis_pigmentes_picociyanin_beauty_cosmetic_micro algea_algea

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Article review of nutritional management in women with polycystic ovary syndrome from 2018 to 2023 (Review)

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Introduction: Poly-cystic ovary syndrome (P COS) is the most common endocrine disorder in women of reproductive age, whose incidence is 12-18% depending on the diagnostic and demographic criteria studied.

Methods: This systematic review, to identify studies aimed at nutritional management in women with PCOS, searched PubMed, Google Scholar, and Science Direct databases based on the keywords Nutrition and poly-cystic ovarian syndrome, Poly-cystic ovarian syndrome, Diet and poly-cystic ovarian. She carried out the syndrome between 2018 and 2023. After checking the title and summary of the articles and removing irrelevant reports, I searched the full text related to the topic included in the study—narrowing the results to English articles on women of reproductive age.

Results: According to the studies, most women with PCOS use a balanced and inappropriate diet, which includes a lack of fiber, omega-3, calcium, magnesium, zinc, and vitamins (folic acid, vitamin C, vitamin B12, and vitamin D). Ali Despite numerous studies, the optimal dietary components for P COS are poorly defined. However, lifestyle management with dietary modification is considered one of the first-line treatments for metabolic syndrome in overweight and obese women with P COS. Should appropriately manage treatment for each patient based on their phenotype, signs, and symptoms.

Conclusion: All women with poly-cystic ovary syndrome should know that healthy lifestyle behaviors, healthy nutrition, and regular physical activity can improve health and well-being by optimizing hormonal results. Finally, the dietary management of women with P COS should be under the joint guidance of nutritionists, gynecologists, fertility specialists, and endocrinologists from the time of diagnosis to help patients.

Keywords: poly-cystic ovary syndrome, nutritional management, die

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Artificial intelligence is a useful collaboration in the field of infertility treatment of female origin: a review study (Review)

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Introduction: In the ever-evolving landscape of healthcare, a remarkable ally has emerged to investigate the cause and treatment of infertility,name is artificial intelligence (AI). Artificial intelligence (AI) can assist in female infertility treatment in several ways, for example :Determining the best treatment for individual infertility patients: Reproductive experts can use AI and machine learning models to determine the most appropriate therapy for infertility patients, increasing successful pregnancy rates and reducing the financial burden.Improving infertility diagnosis and ART outcomes: AI has the potential to improve infertility diagnosis and ART outcomes, estimated as pregnancy and/or live birth rate, especially with recurrent infertility cases.Enhancing in vitro fertilization (IVF) procedures: AI-assisted IVF is a rapidly growing area of research that can improve ovarian stimulation outcomes and efficiency by optimizing the dosage and timing of medication. AI can also help women find good quality eggs to support IVF and egg freezing. AI can assess embryo quality and select the highest quality embryos for fertilization. AI can consistently and effectively identify an embryo with optimal developmental and implantation potential.Predicting pregnancy outcomes: AI can predict the chances of pregnancy in IVF cycles, guiding treatment and reducing the burden of patients.Developing a web-based system for predicting IVF outcome: A proposed web-based system using artificial intelligence can predict IVF outcome by including majority indicators of IVF cycle assessment, such as stimulation protocol, gonadotrophin dose, hormone level, and couple's information.

Methods: The method of this review study was carried out by investigating the articles available in ISI, Scopus, PubMed and Google Scholar .

Results: In summary, AI can assist in female infertility treatment by determining the best treatment for individual patients, improving infertility diagnosis and ART outcomes, enhancing IVF procedures, predicting pregnancy outcomes, and developing a web-based system for predicting IVF outcome

Conclusion: Artificial intelligence (AI) is being increasingly used in the field of infertility treatment, particularly in in vitro fertilization (IVF) procedures. AI is being tested in several areas of reproductive medicine, including sperm identification and morphology, automatic embryo cell stage prediction, embryo evaluation, and prediction of live birth, as well as the development of improved stimulation protocols. AI technology has the potential to improve infertility diagnosis and ART outcomes, estimated as pregnancy and/or live birth rate, especially with recurrent infertility cases. AI can also help expert find good quality eggs to support IVF and egg freezing. AI-assisted IVF is a rapidly growing area of research that can improve ovarian stimulation outcomes and efficiency by optimizing the dosage and timing of medication. AI can also help determine the best treatment for individual infertility patients, increasing successful pregnancy rates and reducing financial burden. AI can assess embryo quality and select the highest quality embryos for fertilization. AI can consistently and effectively identify an embryo with optimal developmental and implantation potential. AI has the potential to enhance the IVF process at every step where decisions are made, and it could potentially be used to help doctors and patients make better-informed choices about additional IVF cycles and oocyte freezing.

Keywords: infertility،female infertilty,Artificial intelligence

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Assesment of Gut Bacterial Profile in Diabetic Patients Undergoing Bariatric Surgeries Using Quantitative PCR" (Research Paper)

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Introduction: Introduction: : In recent years, studies regarding the association of gut microbiome and multifactorial genetic disorders such as diabetes, has gained a lot of traction. Furthermore, metabolites excreted from gut microbiota have broad effects on genes responsible for a wide range of human disorders. The aim of this study was to evaluate changes in gut bacterial load in obese diabetic patients undergoing bariatric surgery.

Methods: Methods: Thirty obese and eligible patients were recruited from the Obesity Clinic of Rasool-E-Akram Hospital Complex in Tehran, Iran between May 2021 to May 2022. Blood and stool samples were collected from patients at two time-points: (1) before surgery (2) 6-months after surgery. These samples were used to determine the effect of the surgery on metabolic indices and gut microbiota via quantitative PCR.

Results: Results: Bariatric surgery showed tremendous potential for alleviating the metabolic imbalance. Analyzing patient subgroups revealed that these surgeries can effectively alter the level and ratio of gut bacteria in diabetic patients with habit of volume eating. In these patients the relative proportion of Bifidobacter to Lactobacillus and Bifidobacterium to total load were decreased, while proportions of Bacteriodetes to Bifidobacterium and Provetella to Bifidobacterium were significantly increased.

Conclusion: Conclusion: Gathered results regarding changes in gut microbiota profile of diabetic patients and alleviation of the existing dysbiosis can be used as a potential therapeutic approach in treatment.

Keywords: Diabetic Patients , Bariatric Surgeries , microbiom

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Assessing the effect of HCT116-released exosomes on mRNA expression level of ATF4, ATF and DDIT3 in peripheral blood mononuclear cells (PBMC) isolated form healthy individuals (Research Paper)

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Introduction: Today, colon cancer is the third most common cancer in the world. According to epidemiologic studies, this cancer is the second and third most common cancer in men and women, respectively. In 2022, cases of incidence and mortality due to this disease is about 1.9 million and 900 thousand people, respectively. One of the mechanisms of immune response regulation by tumor cells is the secretion of extracellular vesicles (EV). Tumor-derived extracellular vesicles (TEX) play a key role in reprogramming the immune system by delivering their cargo to various immune cells. Several studies have shown that tumor-derived exosomes (TEX) play an important role in angiogenesis, tumor growth, Invasion, metastasis, escape from the immune system response through increasing the expression of immune checkpoints and induction of apoptosis in activated CD8+ T cells, suppression of natural killer cells (NK cells), interference in monocyte differentiation and proliferation of Treg and MDSC cells. The things mentioned in relation to the effect of exosomes on the immune system are consistent with the effect exerted by ER Stress. The purpose of this study was to investigate the expression changes of some genes involved in the UPR pathway in peripheral blood mononuclear cells. It is the peripheral blood of healthy people which has been treated with tumor exosomes.

Methods: In this study, HCT-116 cells, which are colorectal cancer cells, were cultured, then tumor exosomes were purified and confirmatory tests were performed to check the presence of exosomes. Then, these exosomes were treated with half of the IC50 concentration obtained from the MTT test on PBMC cells isolated from 6 healthy individuals, and finally, assessing the level of expression of ATF4, ATF6 and DDIT3 genes using qRT-PCR .

Results: In this study, the effect of exosomes of colorectal cancer cell line (HCT-116) was investigated on the expression of ATF4, ATF6 and DDIT3 genes. The expression levels of none of the ATF4, ATF6 and DDIT3 genes were significantly different between the groups treated with exosomes isolated from HCT-116 and exosomes isolated from the complete medium containing 5% FBS and the group treated with PBS (P>0.05)

Conclusion: In general, this study, showed that there is not a significant difference in the expression of ATF4, ATF6 and DDIT3 genes in the PBMC cells of healthy individuals which treated with exosomes extracted from the supernatant of the HCT-116 cell line culture medium compared to the Control groups (group treated with exosomes isolated from complete medium containing 5% FBS and group treated with PBS).

Keywords: HCT116, UPR, PBMC, ATF4, ATF6, DDIT3

Assessing the Utility and Limitations of Nanocomposites in Mental Health Medications: A Comprehensive Review of Advantages and Drawbacks (Review)

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Introduction: Mental health disorders, affecting millions worldwide, remain a global challenge. The quest for more effective treatments has led researchers to explore innovative solutions. One such avenue involves the use of nanocomposites in drug formulations. Nanocomposites, materials combining nanoparticles with pharmaceuticals, offer unique properties that can potentially revolutionize mental health treatment. This article delves into the latest research on the advantages and drawbacks of incorporating nanocomposites into mental health drugs.

Methods: Research on nanocomposites in mental health drugs encompasses a range of approaches. Studies employ materials science, pharmacology, and psychology to investigate the impact of these novel formulations. In vitro and in vivo experiments assess the efficacy and safety of nanocomposite-based drugs. Behavioral assessments and biochemical analyses help evaluate their effects on mental health.

Results: Pros of Using Nanocomposites in Mental Health Drugs: 1. Enhanced Drug Delivery: Nanocomposites enable precise drug targeting to the brain, improving drug efficacy while minimizing side effects. 2. Controlled Release: Nanocomposite formulations can provide sustained drug release, ensuring a consistent therapeutic effect and reducing the need for frequent dosing. 3. Improved Bioavailability: Nanoparticles can enhance the solubility of poorly water-soluble drugs, increasing their absorption and bioavailability. 4. Personalized Medicine: Tailored nanocomposite formulations allow for personalized treatment plans, optimizing outcomes for individuals with unique mental health needs. 5. Reduced Side Effects: Targeted drug delivery reduces exposure to healthy tissues, potentially reducing side effects commonly associated with mental health medications. Cons of Using Nanocomposites in Mental Health Drugs: 1. Safety Concerns: Nanoparticles' potential toxicity and long-term effects on the brain raise safety concerns, necessitating rigorous testing and risk assessment. 2. Regulatory Challenges: The regulation of nanocomposite-based drugs is complex and evolving, requiring clearer guidelines to ensure patient safety and efficacy. 3. Ethical Considerations: The use of nanocomposites in mental health drugs raises

ethical questions about identity, autonomy, and potential misuse. 4. Cost and Accessibility: Developing nanocomposite formulations can be expensive, potentially limiting accessibility for some patients.

Conclusion: Research into nanocomposites in mental health drugs offers promising prospects for improving treatment outcomes while minimizing side effects. Enhanced drug delivery, controlled release, and personalized medicine are among the potential benefits. However, safety concerns, regulatory challenges, ethical considerations, and cost-effectiveness must be carefully addressed. Interdisciplinary collaboration between materials scientists, pharmacologists, clinicians, and ethicists is essential to navigate this evolving field. As research advances, balancing innovation with patient safety and ethical considerations is paramount to realizing the full potential of nanocomposites in mental health drug development. Nanocomposites show great promise in the field of mental health drug development, offering enhanced drug delivery and potential reductions in side effects. However, addressing safety concerns, regulatory challenges, ethical considerations, and cost-effectiveness is critical to ensure that these innovations benefit patients and society as a whole.

Keywords: Nanocomposites, Mental Health, Drug Delivery

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Assessment of Antioxidant Properties of PDA-Coated Curcumin Nanoparticles: A Serial Dilution Study (Research Paper)

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Introduction: Oxidative stress-induced reactive oxygen species (ROS) play a critical role in various diseases, making antioxidants essential in maintaining cellular homeostasis. Curcumin, a natural polyphenolic compound with potent antioxidant properties, has been widely studied for its potential health benefits. However, its limited bioavailability hinders its therapeutic efficacy. To address this challenge, we synthesized polydopamine (PDA)-coated curcumin nanoparticles and assessed their antioxidant effects at various concentrations. We hypothesized that the antioxidant potential of these nanoparticles would increase with higher concentrations.

Methods: PDA-coated curcumin nanoparticles were synthesized and characterized at 25°C. Six serial dilutions (1/2 dilution each) were prepared using water, resulting in a range of nanoparticle concentrations. The antioxidant properties of each sample were evaluated using two distinct methods: UV-Vis spectrometry and the Fenton reaction, involving the generation of ROS by Fe2(SO4)3 and their subsequent scavenging by salicylic acid. ROS clearance was quantified for each concentration.

Results: Our results demonstrated a clear concentration-dependent increase in the antioxidant properties of PDA-coated curcumin nanoparticles. UV-Vis spectrometry revealed a gradual rise in ROS scavenging capacity as the nanoparticle concentration increased. The ROS clearance values for the six concentrations were 0.45, 0.33, 0.31, 0.23, 0.22, and 0.21, respectively. This trend was further validated using the Fenton reaction method, which consistently showed enhanced ROS scavenging with higher nanoparticle concentrations. The observed dose-dependent effect supports our hypothesis that the antioxidant potential of PDA-coated curcumin nanoparticles is positively correlated with their concentration.

Conclusion: In this study, we successfully synthesized PDA-coated curcumin nanoparticles and demonstrated their increased antioxidant properties with rising concentrations. These findings suggest the potential utility of these nanoparticles as an efficient antioxidant delivery system. The ability to enhance the bioavailability and antioxidant activity of curcumin through nanoparticle formulation holds promise for various therapeutic applications, particularly in combating oxidative stress-related diseases. Further research is warranted to explore the translational potential of these nanoparticles in vivo and their specific mechanisms of action.

Keywords: Curcumin nanoparticles, Antioxidant properties, Polydopamine coating, ROS scavenging

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Assessment of the palmitic acid effect on neural cell lines in Alzheimer's disease: with a comprehensive focus on signaling pathways (Review)

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Introduction: Alzheimer's disease (AD) is characterized by progressive neurodegeneration and cognitive decline. While the exact causes remain unclear, there is increasing evidence that dietary and metabolic factors are implicated in AD pathogenesis. Saturated fatty acids such as palmitic acid (PA), the most common saturated fatty acid in the Western diet, have been shown to have noxious effects on neuronal health. PA can induce neurotoxicity by increasing oxidative stress, altering amyloid precursor protein processing, and promoting tau phosphorylation. In vitro studies with neuronal cell lines have demonstrated that consumption of PA can impair neuronal viability, plasticity, mitochondrial function, etc. through several potential mechanisms, including endoplasmic reticulum stress, autophagy dysregulation, and activation of inflammatory pathways. Comprehensive assessment across diverse neural cell models is necessary to elucidate the effects of PA on neurons and glial cells that underlie AD development. This review evaluates deleterious actions of PA in neural cells with a comprehensive concentration on signaling pathways which is crucial to elucidating diet-derived risk factors and guiding new preventative approaches for AD.

Methods: This review was conducted for articles published in ScienceDirect, Scopus, and PubMed from January 1, 2017, to December 31, 2022. The search strategy was performed using a combination of terms based on palmitic acid, neural cell lines, Alzheimer's disease, and other related words for titles/abstracts. Two independent reviewers skimmed the titles and abstracts for eligibility criteria and relevant articles were included. Unrelated and non-English articles were excluded and a table was designated for excluded articles.

Results: PA has effects on neural cells and has been implicated in the pathogenesis of AD. It disrupts several signaling pathways involved in

homeostasis, metabolism, plasticity, protein aggregation and phosphorylation, and neuronal survival, and can lead to AD neurodegeneration. These signaling pathways include the following: (1) the endoplasmic reticulum (ER) stress pathway disrupts ER calcium homeostasis and protein folding, leading to activation of the unfolded protein response. (2) Inflammatory pathways involving NF-κB and MAPK signaling in astrocytes and microglia. These cells release cytokines, which cause neural damage. (3) Oxidative stress pathways increase reactive oxygen species (ROS) and impair antioxidant defenses. In contrast, impaired neuroplasticity depends on insulin signaling, which triggers (4) PI3K/Akt and MAPK/ERK pathways. It should be noted that the activation of caspase-3 and Bcl-2 family proteins stimulate (5) mitochondrial apoptosis pathways in neurons. Besides, (6) the autophagy pathway dysregulates autophagic flux in neurons and impairs the clearance of protein aggregates, such as amyloid-beta. The foremost critical signaling pathway is elevated (7) tau phosphorylation, which has a reciprocal function by enacting glycogen synthase kinase 3β (GSK3β) and inhibiting protein phosphatase 2A (PP2A). Finally, PA can reduce (8) BDNF/TrkB signaling, which is involved in neuronal survival and plasticity.

Conclusion: As mentioned above, PA profoundly impacts AD-related crucial signaling pathways by disruption in neural metabolism, plasticity, and survival. The article, emphasizes the potential dietary and therapeutic implications based on the results. PA demonstrates stress level in ER, stimulates inflammatory pathways, increases oxidative stress, attenuates neuronal insulin signaling, activates apoptotic cascades, dysregulates autophagy, promotes tau hyperphosphorylation, and finally reduces BDNF/TrkB signaling. Limiting dietary intake of PA may therefore represent an accessible preventative strategy to reduce risk factors for sporadic AD. Furthermore, the development of targeted therapeutics to counteract the signaling disruptions triggered by PA in the brain may open new opportunities to halt neurodegeneration in the early stages of AD. Further research is still needed to fully elucidate the correlation between this prevalent dietary saturated fatty acid and the complex molecular pathways underpinning AD progression.

Keywords: Palmitic Acid, Cell Line, Neurons, Alzheimer Disease, Signal Transduction, signaling pathway

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Association between cardiometabolic risk factors and COVID-19 susceptibility, severity and mortality: a review (Research Paper)

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Introduction: The latest pandemic of the coronavirus has affected all components of the human lifestyles and has unfolded the sickness rapidly at some stage in the world. The coronavirus disease of 2019 (COVID-19) has been recognized as 2019-nCOV. This novel virus motives COVID-19 ailment that has comparable signs and symptoms as severe acute respiratory syndrome coronavirus 2 (SARS-COV2). Since April 10, 2021, a total number of 135 Million cases of COVID-19 occurring in at least 170 countries and territories were reported with relatively 3–4% of fatality rate. Although not all factors affecting mortality and severity of COVID-19 disorder have now been identified, studies have shown that the majority of mortality were amongst patients of > 60.Due to the high incidence of cardio metabolic risk factors in the world population and other roles in changing the course of many diseases, in this study, which is a narrative review article [3], we decided to review the role of COVID-19 and recent pandemic in altering these risk factors such as HTN, DM, dyslipidemia and obesity along with the impact of these metabolic comorbidities in the course of COVID-19 disease in infected people.

Methods: In this study, we aimed to review the articles from the beginning of the pandemic on the impression of cardio metabolic risk factors on COVID-19 and the effectiveness of COVID-19 on how to manage these diseases. All the

factors studied in this article, including hypertension, diabetes mellitus, dyslipidemia, and obesity exacerbate the course of Covid-19 disease by different mechanisms, and the inflammatory process caused by coronavirus can also create a vicious cycle in controlling these diseases for patients.

Results: Due to the predominance of individuals with cardio metabolic illnesses, in this pandemic, we decided to review articles on the impact of cardio metabolic risk factors on coronavirus disease 2019 and the viability of coronavirus within the course of cardio metabolic diseases. Various studies revealed the association between the severities of COVID- 19 infection in individuals with hypertension besides the higher frequency of this infection in these people. Most of the articles looked into in this paper concurred on continuing treatment with ACEI or ARB (as the foremost common antihypertensive drugs) during this pandemic and after getting COVID-19 disease. Diabetes is another cardio metabolic risk factor that in this article is perceived as one of the factors that exacerbated COVID-19 infection, but autonomously was not a factor in increasing the chance of developing the disease. Dyslipidemia is a viable factor within the occurrence of myocardial infarction as well as stroke, and is known as a cardio metabolic risk factor impacting human wellbeing. Dyslipidemia affects the COVID-19 infection in several ways, including the level of HDL as a prognostic risk factor of COVID-19 disease severity by multiple components which has been clarified in detail before. There's a controversy over using statins in COVID-19 infected patients but a plenty of research have supported the usage of these drugs in these patients. Obesity is an epidemic of the last century that in conjunction with the coronavirus pandemic can play an important role in changing the course of this infectious disease. The ACE2 expression in adipose tissue is higher than that in the lungs as a major target organ by COVID-19 implying that adipose tissue may be more vulnerable to COVID-19 infection.

Conclusion: In general, due to the high prevalence of cardiometabolic diseases, especially in the population over 60 years old, it seems that these diseases have contributed to the worsening of COVID-19 disease in a recent pandemic, and monitoring these cardiometabolic risk factors can improve the course of COVID-19 infections and could be beneficial generally.

Keywords: COVID-19 · Cardio Metabolic Risk Factors · Dyslipidemia · Diabetes mellitus · Hypertension · Obesity

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Association between Helicobacter pylori Infection and Primary Open-Angle Glaucoma: A Systematic Review and Meta-Analysis (Review)

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Introduction: Purpose: This systematic review and meta-analysis summarizes the evidence for the association between Helicobacter pylori infection and primary open-angle glaucoma.

Methods: Methods: Eligible studies reporting an association between H. pylori infection and glaucoma were identified through an extensive search of the Excerpta Medica (EMBASE), Web of Science, Scopus, and PubMed databases, and a review of the reference lists of top articles up until October 2022. The analysis was performed using a random effects model in Stata 17.

Results: Result: The systematic review included 24 studies, comprising 1602 glaucoma patients and 2800 control individuals. The combined relative risks (RRs) of cohort studies and overall combined odds ratios (ORs) of case-control studies demonstrated a significant correlation between H. pylori infection and glaucoma. Subgroup analysis revealed that glaucoma patients had a higher risk of H. pylori infection if they were residents of European countries (Cohort: RR: 1.69; 95% CI: 1.3-2.19) and (Case-Control: RR: 3.71; 95% CI: 2.07-6.64), had primary open-angle glaucoma (POAG) (Cohort: RR: 1.76; 95% CI: 1.37-2.27) and (Case-Control: RR: 3.71; 95% CI: 2.93-4.70), were diagnosed with H. pylori infection using histology (Cohort: RR: 1.95; 95% CI: 1.26-3.01) and (Case-Control: RR: 4.06; 95% CI: 2.28-7.22), and were over 60 years old (Cohort: RR: 1.63; 95% CI: 1.33-2.00) and (Case-Control: RR: 2.95; 95% CI: 2.27-3.83).

Conclusion: Discussion: The meta-analysis results suggest a statistically significant association between Helicobacter pylori infection and primary open-angle glaucoma.

Keywords: Helicobacter Pylori, Glaucoma, Primary Open-Angle Glaucoma, Pseudo-Exfoliation Glaucoma

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Association of COL7A1 gene polymorphisms with risk of dystrophic epidermolysis bullosa. A systematic review and meta-analysis (Review)

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Introduction: Epidermolysis bullosa (EB) is an inherited, heterogeneous group of rare genetic dermatoses characterized by mucocutaneous fragility and blister formation, inducible by minimal trauma (1). It has four major categories, based usually on the plane of cleavage within the skin and reflecting the underlying molecular abnormality: EB simplex, junctional EB, dystrophic EB and Kindler EB. The most feared of which — and also the leading cause of mortality — is squamous cell carcinoma (1). According to the layer of skin in which blistering occurs: epidermolysis bullosa simplex (intra epidermal), junctional epidermolysis bullosa (within the lamina lucida of the basement membrane), dystrophic epidermolysis bullosa (below the basement membrane), and Kindler epidermolysis bullosa (mixed skin cleavage pattern) (2). Pathogenic variants in at least 16 genes that encode proteins vital for the integrity and adhesion of skin layers have already been associated with different subtypes of epidermolysis bullosa (2). The deficiency and/or dysfunction of type VII collagen leads to subepidermal blistering immediately below the lamina densa, resulting in mucocutaneous fragility and disease complications such as intractable ulcers, extensive scarring, malnutrition, and malignancy (3). The disease is predominantly diagnosed by immunofluorescence mapping and/or transmission electron microscopy and subsequently subclassified into one of 14 subtypes (3). Dystrophic epidermolysis bullosa (DEB) is inherited in both an autosomal dominant DEB and autosomal recessive manner RDEB, both of these result from mutations in the type VII collagen gene (COL7A1). Dominant dystrophic epidermolysis bullosa predominantly involves glycine substitutions within the triple helix of COL7A1 although other missense mutations, deletions or splice-site mutations may underlie some cases (4). In recessive dystrophic epidermolysis bullosa, the mutations include nonsense, splice site, deletions or insertions, ‘silent’ glycine substitutions within the triple helix and non-glycine missense mutations within the triple helix or non-collagenous NC-2 domain (4). Procollagen VII is a homotrimer composed of three proa1 (VII) chains which

are encoded by the 32 kbCOL7A1gene located on chromosome 3p21. The mRNA transcript of approximately 8.9 kb is translated into a proa1 (VII) polypeptide containing 2944 amino acids (4). RDEB is caused by mutations to the COL7A1 gene located on chromosome three. A lack of type VII collagen protein at the dermal-epidermal junction (DEJ) results in a loss of structural integrity of the skin. Patients with RDEB exhibit incurable, often fatal, skin blistering, and have an increased risk for aggressive squamous cell carcinoma (5).

Methods: Study identification and selection: This meta-analysis conformed to the Preferred Reporting Items for and Meta-analyses criteria. Two investigators independently searched the databases MEDLINE (PubMed), Google Scholar, Web of Science (Thomson-Reuters), for eligible articles examining the association COL7A1 gene polymorphisms with risk of Dystrophic Epidermolysis Bullosa published up to August 4, 2023. The following terms were used: (“Dystrophic Epidermolysis Bullosa”) AND (“COL7A1” OR “Collagen alpha-1(VII) chain’’) AND (“rs2532848”) AND (“rs9878950”) AND (“rs9814951”) AND (“rs9871180”) AND (“rs9881877”) AND (“rs1264194”) AND (“rs2228561”) AND (“polymorphism”, OR “mutation” OR “variant” OR “gene” OR “genotype” OR “SNP” OR “allele”). Additionally, searching of the references of eligible studies, reviews and related meta-analyses, and the abstracts presented at relevant conferences was performed to identify potentially relevant studies. Inclusion and exclusion criteria: Studies were selected according to the following inclusion criteria: (1) full-text published studies up to August 4, 2023; (2) a case-control design or Clinical Trial; (3) the study goal was to evaluate the association of COL7A1 rs2532848, rs9878950, rs9814951, rs9871180, rs9881877, rs1264194, rs2228561 polymorphisms with risk of; Dystrophic Epidermolysis Bullosa, (4) sufficient data for estimating 95% confidence interval (CI) and odds ratio (OR). Data extraction: Information was extracted from all the eligible studies independently by 5 researchers using a pre-designed form according to the selection criteria listed above. For each study the following information was extracted: name of first author, publication year, country where the study was conducted, racial descent, polymorphisms, genotypic testing method, number of cases and controls, genotype frequency of cases and controls, and result of Hardy-Weinberg equilibrium test in control subjects.

Results: 10 records were found after examining online databases, references, and related articles; 9 of these records were subsequently eliminated as being unrelated. The current meta-analysis also included 1 eligible study. Spanish authors produced the included study. Table 1 provides basic data, including SNPs, Position, and Allele. Nine single nucleotide

polymorphisms (SNPs) across the COL7A1 gene were genotyped to create haplotypes. Both control samples and RDEB patients, both of Hispanic ancestry, had their haplotypes identified. In this investigation, sixteen distinct haplotypes were found. an individual carrying the c.6527insC mutation. All bearers of the c.6527insC mutation shared the same haplotype (CCGCTCAAA_6527insC), according to haplotype analysis, pointing to a common ancestor. SNP Position Allele Ref rs2532848 Intron103 C > A (6) rs9878950 Intron93 A > G rs9814951 Intron85 A > G rs9871180 Intron 79 C>T rs9881877 Intron 70 C>T rs1264194 Exon 90 A > G rs2228561 Exon19 C>T

Conclusion: Several studies have examined associations between COL7A1 gene polymorphisms and risk of Dystrophic Epidermolysis Bullosa, but the results were controversial. Meta-analysis has been recognized as a prominent tool to exactly define the effect of genetic polymorphism on the risk of diseases. The present meta-analysis was carried out by critically reviewing 11 relevant and new recently published studies on COL7A1 polymorphisms with Dystrophic Epidermolysis Bullosa risk. Therefore, it may provide more information. The overall distribution of the estimated polymorphisms (Table1) were significantly different between patients and healthy controls.

Keywords: Epidermolysis bullosa, mutations, single nucleotide polymorphisms, COL7A1, type VII collagen

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Association of increased UBE2C expression with disease stage in the development of malignancy and targeted treatment of patients with Hepatocellular carcinoma (HCC) (Review)

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Introduction: Hepatocellular carcinoma (HCC) is the fifth most common cancer in men, the seventh most common cancer in women and the third leading cause of cancer death. Typically, HCC is often diagnosed in advanced stages, and many patients with advanced stages do not qualify for treatment.

Methods: TCGA data were used to identify the expression of altered genes in (HCC) and the relationship between gene expression and patients' stage size. For this purpose, OncoDB database was used and gene expression was normalized by TMP method. To compare the groups, cancer samples were initially evaluated compared to normal. Also, Stage of the disease is divided into 4 categories: Stage I, Stage II, Stage III, Stage IV. Stage I means the disease is only in one area. It is also called early stage cancer. Stages II and III mean that the cancer is larger and has grown into nearby tissues or lymph nodes. Stage IV means that the cancer has spread to other parts of your body.

Results: The results showed that the difference in expression between cancer samples compared to normal showed that 204 genes increased significantly (P <0.001) and with the criterion of | LogFC |> 2 (more than 4 times). On the other hand, the results of examining the relationship between gene expression and patients 'stage showed that the expression of 634 genes was related to patients' stage (P <0.0001). Common genes were identified between the previous stages and the results showed that there were 11 genes that had both increased expression and were associated with patients' stage. UBE2C expression was significantly higher in samples with higher stage compared to stage I and stage II.

Conclusion: Our results showed that the expression of UBE2C in cancer samples with more stage is much higher than the control and tumor samples with lower stage. These results suggest that UBE2C may be a good candidate for targeted treatment for patients with liver cancer. There may also be an increased risk of (HCC) associated with higher stages by increased expression of the UBE2C gene.

Keywords: Hepatocellular carcinoma , UBE2C, Cancer stages, Gene expression changes

Association of Polyunsaturated Fatty Acid Intake on Inflammatory Gene Expression and Multiple Sclerosis: A Systematic Review and Meta-Analysis (Review)

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Introduction: The health benefits of omega-3 fatty acid (FA) supplementation on inflammatory gene expression (IGE) and multiple sclerosis (MS) are becoming more evident. However, an overview of the results from randomized controlled trials is lacking. This study aimed to conduct a meta-analysis to evaluate the effect of omega-3 fatty acid intake on MS (based on the criteria of the Expanded Disability Status Scale (EDSS)) and inflammatory gene expression (IGE).

Methods: A search was conducted of PubMed, EMBASE, and Web of Science for cohort studies published from the inception of the database up to May 2022 that assessed the associations of omega-3 polyunsaturated fatty acids (n-3 PUFAs), docosahexaenoic acid (DHA), α-linolenic acid (ALA), and eicosapentaenoic acid (EPA) with EDSS and inflammatory gene expression (peroxisome proliferator-activated receptor gamma (PPAR-γ), tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), interleukin-6 (IL-6), and interleukin-8 (IL-8)) outcomes. For the highest vs. lowest comparison, the relative risk (RR) estimates with a 95% confidence interval (CI) were pooled using the random-effect model.

Results: In total, 13 cohort studies with 1353 participants were included in the meta-analysis during periods of 3 to 144 weeks. A significant inverse

relationship was found between DHA and EDSS scores (RR: 1.05; 95% CI: 0.62, 1.48; $p < 0.00001$). Our results also showed that omega-3 FAs significantly upregulated the gene expression of PPAR-γ (RR: 0.95; 95% CI: 0.52, 1.38; $p < 0.03$) and downregulated the expression of TNF-α (RR: −0.15; 95% CI: −0.99, 0.70; $p < 0.00001$) and IL-1 (RR: −0.60; 95% CI: −1.02, −0.18; $p < 0.003$). There was no clear evidence of publication bias with Egger's tests for inflammatory gene expression ($p = 0.266$). Moreover, n-3 PUFAs and EPA were not significantly associated with EDSS scores ($p > 0.05$).

Conclusion: In this meta-analysis of cohort studies, blood omega-3 FA concentrations were inversely related to inflammatory gene expression (IGE) and EDSS score, which indicates that they may hold great potential markers for the diagnosis, prognosis, and management of MS. However, further clinical trials are required to confirm the potential effects of the omega-3 FAs on MS disease management.

Keywords: gene expression, multiple sclerosis, ESDD, PPAR family, omega-3

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AT-MSC Exosome: Bone Regeneration (Review)

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Introduction: Adipose tissue MSCs, or mesenchymal stem cells, have been found to be highly effective in promoting bone regeneration. In recent years, a growing body of research has suggested that the therapeutic action of MSCs may be mediated by the secretion of small vesicles, known as exosomes. Exosomes are nanoscale lipid bilayer vesicles that transfer bioactive molecules, including proteins, RNAs, and lipids, between cells. They have been found to play diverse roles in intercellular communication, such as in immune regulation and tumor metastasis. Studies have shown that exosomes released by adipose tissue MSCs (AT-MSCs) have potent effects on bone regeneration and may represent a new therapeutic approach for various bone disorders. One recent study published in the Journal of Tissue Engineering and Regenerative Medicine investigated the effects of AT-MSCs derived exosomes on bone regeneration in vitro and in vivo. The findings showed that AT-MSCs derived exosomes significantly enhanced the osteogenesis of human bone marrow stromal cells, as evidenced by increased cell viability, alkaline phosphatase activity, and calcium deposition. Furthermore, the exosomes also promoted bone regeneration in a rat model of femoral fracture, as assessed by micro-CT analysis and histological staining. Another study published in Stem Cell Research & Therapy demonstrated the therapeutic potential of AT-MSCs derived exosomes for osteonecrosis of the femoral head (ONFH), a devastating disease that often leads to joint destruction and disability. The researchers found that treatment with AT-MSCs derived exosomes significantly improved the survival of osteocytes and the repair of the femoral head in a rabbit model of ONFH. The exosomes also reduced the levels of inflammatory cytokines and enhanced the expression of growth factors in the affected tissues. Overall, these studies suggest that AT-MSCs derived exosomes represent a promising strategy for bone regeneration and may have clinical applications in the treatment of various bone disorders. However, further research is needed to optimize the isolation and characterization of exosomes, as well as to elucidate the mechanism of action and safety profile of exosome-based therapies. With the ongoing development of exosome-based technologies, it is expected that these tiny vesicles will continue to attract increasing attention in the field of regenerative medicine.

Methods: All data is based on recent published articles on PubMed, Google Scholar, and The Life Sciences Journal.

Results: Based on scientific researches, there is mounting evidence that adipose tissue-derived exosomes can enhance bone regeneration. These exosomes contain various functional molecules, such as growth factors, cytokines, miRNAs, and proteins, which modulate cellular processes and regulate the immune response. Studies have shown that adipose tissue-derived exosomes can stimulate osteogenesis, angiogenesis, and anti-inflammatory responses, which promote bone healing and regeneration.

Conclusion: In conclusion, this review will provide a comprehensive analysis of the potential of adipose tissue MSCs derived exosomes for bone regeneration. The results of this study will be of great importance for developing novel tissue engineering strategies for bone healing and repair.

Keywords: Adipose Tissue Mesenchymal Stem cells, Exosome, Bone regeneration, regenerative medicine, Stem Cells

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Atorvastatin Inhibits Viability and Migration of MCF7 Breast Cancer Cells (Research Paper)

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Introduction: Atorvastatin is commonly used as a lipid-lowering drug. The emerging interest in statins as anticancer agents is based on their pleiotropic effects on cancer cells. Among the statins, atorvastatin, and in cancers, breast malignancies have received less attention in preclinical investigations. In order to enhance the efficacy of cancer treatment, adjuvant, less expensive therapeutic strategies have been recently noticed. In this case, we investigated the in-vitro effect of atorvastatin on the viability and migration of the MCF7 breast cancer cell line.

Methods: We tested the cytotoxicity of atorvastatin on breast cancer cell survival by MTT assay. Annexin-V / PI staining and then flow cytometry of cancer cells in addition to quantitative real-time PCR tests quantified the apoptosis and necrosis of cancer cells. We figured out the impact of atorvastatin on cancer cell migration capability through scratch-wound healing assay and transwell migration examination. Inverted light microscope and fluorescent imaging displayed the morphological changes following treatment of MCF7 cells with atorvastatin.

Results: We concluded that atorvastatin can trigger MCF7 cancer cells to undergo necrosis and caspase-dependent apoptosis based on the viable/dead cell number, mitotic cell cycle, gene expression, and morphological assays. The results were dose- and time-dependent and the half-maximal inhibitory concentration of atorvastatin for cancer cells' viability inhibition was 9.1 μM/L(nM/mL). Moreover, the migration of MCF7 cells was inhibited in the treated group as we figured out in two- and three-dimensional migration methods.

Conclusion: In-vitro inspection of drug-cancer cell interactions paves the way for future in-vivo research studies. These in-vitro results revealed that atorvastatin has anti-viability and anti-migration effects on breast cancer cells.

Keywords: Statin, MCF7Cell line, Migration, Apoptosis

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Battling the Antibiotic Resistance Crisis (Review)

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1.

Introduction: Antibiotic resistance is a critical global health threat, potentially causing millions of annual fatalities in the near future due to the overuse of antibiotics, leading to the emergence of drug-resistant bacteria. Researchers are responding by exploring innovative "resistance-resistant" therapeutic strategies.

Methods: review

Results: These include using compounds to reduce mutagenesis, employing antibiotic cycling and evolutionary steering to make bacteria more susceptible, and developing combination therapies to target defensive mechanisms. Future directions involve leveraging machine learning and personalized medicine. This review also emphasizes the urgency of curbing antibiotic resistance in humans, offering strategies such as reducing colonization by drug-resistant bacteria, enhancing colonization resistance, and mitigating the transfer of resistance genes.

Conclusion: Adopting an interdisciplinary one-health approach is crucial for comprehensive bacterial resistance prevention and control.

Keywords: Antibiotic resistance, Resistance-resistant, Antibiotic cycling

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Beneficial effects of caffeic acid in improving the symptoms of ulcerative colitis experimental model in Wistar rats (Research Paper)

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Introduction: This investigation assessed the influence of Caffeic Acid (CA) on the principal immunological responses in a mouse model of Ulcerative Colitis (UC). Owing to its cardioprotective, antiviral, antioxidant, antitumor, anti-inflammatory, and antimicrobial properties, CA is significant owing to its wide-ranging consumption in the standard human diet. Therefore, it's anti-inflammatory and anti-cancer attributes pave the way for it to be perceived as a potential alternative approach to prevent inflammatory and colorectal cancer diseases.

Methods: In this study, we classified 28 adults male Wistar rats randomly into four sets of seven, encompassing a healthy control group, a diseased control group, a unit receiving prednisolone treatment (2 mg/kg PO), and a unit receiving caffeic acid treatment (150 mg/kg PO). UC was initiated in rats through the rectal administration of acetic acid. Following the confirmation of disease initiation, rats were subjected to a 10-day treatment phase during which the respective group animals received their treatments. At the conclusion of the treatment phase, rats were humanely euthanized, and serum and colon tissue samples were harvested. The expression of inflammatory genes TNF-α, IL-1, and IL-6 in homogenized colon tissue samples was assessed, and disease severity and tissue inflammation were gauged by measuring the level of total protein.

Results: The study's outcomes suggest that both treatment methodologies, namely CA and the traditionally used prednisolone, are effective in mitigating the severity and enhancing the clinical symptoms of UC. CA was discerned to notably diminish the levels of inflammatory cytokines interleukin-1 beta, interleukin-6, and TNF-alpha, as well as total protein in the serum, suggesting its potential for reducing disease severity. Furthermore, CA was found to be superior to prednisolone in reducing the escalated levels of interleukin-1 beta and TNF-alpha, respectively.

Conclusion: In conclusion, these findings endorse the notion that Caffeic Acid could be considered a natural therapeutic strategy for alleviating the symptoms of Ulcerative Colitis.

Keywords: Ulcerative Colitis, Caffeic Acid, Anti-Inflammatory effects, Rat Wistar

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Beneficial effects of Mangifera indica L extract in reducing symptoms of experimental ulcerative colitis model (Research Paper)

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Introduction: In this experimental study, we investigated the clinical effects and immune responses of the hydroalcoholic extract of Mangifera indica L (MIE) in an animal model of ulcerative colitis. Mangifera indica L, commonly known as mango, is a fruit rich in tannins that has been proposed as a potential alternative strategy for the prevention of auto-inflammatory diseases and colon cancer due to its anti-inflammatory properties.

Methods: We randomly assigned thirty-two adults male Wistar rats into four groups of eight, including a healthy control group, a patient control group, a patient group receiving prednisolone (2 mg/kg PO), and a group receiving mango extract (150 mg/kg PO). Ulcerative colitis was induced in the rats by intrarectal injection of acetic acid. After confirming the induction of the disease, the rats underwent a ten-day treatment period during which animals in the gavage groups were administered their respective treatments. At the end of the treatment period, the rats were euthanized in a humane manner, and blood serum and colon tissue samples were collected.The obtained results were analyzed using one-way analysis of variance and disease activity index, anti-inflammatory activity were evaluated by measuring tissue myeloperoxidase (MPO) activity, colon tissue lipid peroxidation (MDA) levels using thiobarbituric acid reactive substances (TBARS), and tissue nitric oxide (NO) activators. Additionally, disease severity and tissue inflammation were assessed by measuring total protein levels.

Results: The results of this study indicate that both treatment modalities, namely plant extract and prednisolone, exhibited efficacy in reducing the intensity of clinical symptoms associated with ulcerative colitis.In the study, it was observed that Mangifera indica L extract displayed significant anti-inflammatory properties. The extract was found to decrease the elevated levels of MPO, NO, MDA, and total protein in the blood serum with a

significant difference, which suggests its potential for reducing the severity of the disease. Additionally, the study found that Mangifera indica L extract was more effective than prednisolone in reducing the increased levels of MDA and total protein in the blood serum with a significant difference.

Conclusion: Notably, treatment with Mangifera indica L plant extract is associated with fewer side effects compared to prednisolone. Overall, these data support the notion that Mangifera indica L extract may be utilized as a natural-source treatment strategy for reducing the symptoms of ulcerative colitis.

Keywords: Ulcerative Colitis, herbal extract, Anti-Inflammatory effects, Mangifera indica L,Wistar rats.

Benifit of Laparoscopy in ventriculoperitoneal Shunt Placement in hydrocephalus patients (Review)

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Introduction: Basically the managing patient with hydrocephalus and helping them before irreversible effect on their brain function at the same time reduce compilations after the shunt surgery is making the situation too hard for them. So base on new methods and instrument that is useful for lowering the risks of infections and malfunction shunt. there is lots of article that completely covers the complication with percentage of each of them but this review mostly focused on new methods and protocols . Laparoscopy is one of them in reducing chance of postoperative malposition and obstruction in shunt terminal, and it shows approximately after 1 year in one third of patients, the laparoscopy for distal catheter is doing recently with 3 different method Suture and ligature under laparoscope, Titanium clip fixation under laparoscope and Subcutaneous fixation under laparoscope , the moment shows csf derange from cranial the laparoscope is getting remove, and this methods use in average age range: 9–81 years and the result 93.3% (28/30) succession of subcutaneous fixation, this is better option in comparing with open surgery this method will help faster recovery and low chnce of obstracture because the catheter will place in the suprahepatic space and the fixation will help to not get dislocation and malposition.

Methods: And as in open surgery there is some complication in damage to liver, vagina, urinary bladder, gallbladder and bowel, that will not appear in this method. Diaphragmatic CSF Fistula is the other complication that lead to chronic plural effusion was seen in vp shunt is a rare complication, plural effusion can be with or without migration(the correct position of the distal part of the VP shunt) shunt insertion is another common complication in vp shunt receivers, often after 2 to 9 years will appear , with skin rush , pain and irritation that is a result of calcification shunt, that will lead to total shunt removal unfortunately Removal is dangerous. but in this study they offers a method to remove the calcified tissue without removing the shunt to just only relief the pain and help the patient life , other operation can be applying for ETV and whom doesn’t fit with this operation can apply for inserting another

VP shunt on the other side in case of intracranial calcification shunts ,mostly the common site was in neck ,the abdomen and chest.

Results: in other research among 405 cases shows for seeing more advantage and disadvantage result among them, with 2 to 9 years follow up after the surgery , almost 0 peritoneal catheter misplacement and only in 2 case saw injury of the small bowel that get repair immediately and 2 case umbilical hernia ,was only complications that appear, other good things about this method is short time of surgery and fast recovery with less anesthetic medication because of short operative procedure and direct laparoscopic vision to manage the shunt location intraperitoneally was the key of the operation so the patients will be less under effect of radiology exposures.

Conclusion: using the laparoscopy this invasive method for insert the vp shunt in abdomen to facility the operation in this article they did for all patient in Neurosurgical Department of AHEPA Hospital that needs vp shunt with using laparoscopy the result was excellent , facility of recovery after surgery no complication during and after surgery, high safety percentage , Under direct visibility, the surgeon can check that the abdominal component of the VPS locates to the proper place and that CSF flow is adequate. this method definitely is better and old traditional open abdominal operations .the patient was taking orally food without any pain or vomiting , this method with reduce the chance of adhesions and ileus after surgery.

Keywords: Vp shunt, ,Complications, Hydrocephalus,Laparoscopic surgery

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Beyond Tyrosinase: Understanding the molecular Insights and Functional Significance of TRP-1 and TRP-2 in Hyperpigmentation (Review)

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Introduction: Hyperpigmentation is a prevalent dermatological condition characterized by the overproduction and deposition of melanin in the skin. Tyrosinase-related proteins 1 (TRP-1) and 2 (TRP-2), also known as dopachrome tautomerase (DCT), are key players in the melanin synthesis pathway. In this review, we aim to explore the structure and role of TRP-1 and TRP-2 in hyperpigmentation. Understanding the involvement of these proteins will shed light on the underlying mechanisms and potential therapeutic strategies for hyperpigmentation disorders.

Methods: A comprehensive literature search was conducted using databases such as PubMed, Scopus, and Web of Science. The search terms included "tyrosinase-related proteins 1," "TRP-1," "tyrosinase-related proteins 2," "TRP-2," "hyperpigmentation," and related keywords. Only English-language, full-text articles focusing on the structure and role of TRP-1 and TRP-2 in hyperpigmentation were included. Selected articles were assessed for their relevance to the topic and the quality of evidence presented.

Results: The literature review revealed that TRP-1 and TRP-2 are critical components of the melanin synthesis pathway in melanocytes. TRP-1, a glycoprotein, is primarily involved in the maturation and stabilization of melanin. It plays a key role in eumelanin production and contributes to the brown-black pigmentation of the skin. On the other hand, TRP-2, a multifunctional enzyme, participates in the conversion of dopachrome to 5,6-dihydroxyindole-2-carboxylic acid (DHICA), a precursor of both eumelanin and pheomelanin. TRP-2 also exhibits antioxidant properties and is involved in melanosome transport and melanin deposition.

Conclusion: The structural characteristics of TRP-1 and TRP-2 enable their crucial functions in the melanin synthesis pathway and contribute to the complexity of hyperpigmentation. Dysregulation of TRP-1 and TRP-2 expression and activity has been linked to hyperpigmentation disorders,

including melasma and post-inflammatory hyperpigmentation. Understanding the specific roles of TRP-1 and TRP-2 in hyperpigmentation may provide insights into potential therapeutic targets. Strategies to modulate the activity or expression levels of TRP-1 and TRP-2 could hold promise for the treatment of the mentioned disorders.

Keywords: TRP-1 , TRP-2 , hyperpigmentation, dopachrome tautomerase

Biofilm formation and prevalence of integrons and ESBL genes and FimH gene in multidrug resistant uropathogenic Escherichia coli isolated from urinary tract infections (Review)

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Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections globally, influencing 150 million individuals every year around the world. Uropathogenic Escherichia coli (UPEC) is the most common causative agent of UTI. Emergence of multidrug-resistant isolates is the caused by excessive and inappropriate use of antibiotics. UPEC generally use various adhesins to binding and invading bladder cell. Type 1 fimbriae (FimH) is one of the most common fimbriae appear to play a role in inter-bacterial binding and biofilm formation. In fact biofilm formation seems provides an promoted growth and persistence of bacteria resulting in resistance to antibiotics. Integrons are mobile genetic elements play that important role in the development of antibiotic-resistance strains. On the other hand, extended-spectrum beta lactamase (ESBL) are a group of enzymes that usually resistant to various antibiotics. The ESBL genes can be carried by integron-containing isolates to make them multidrug resistance.

Methods: The prevalence of class 1, 2, 3 integrons and ESBL genes and fimH gene was verified by the PCR method. Antimicrobial susceptibility of UPEC isolates was performed using disc diffusion method. and biofilm formation was investigated using microtitre plate assay.

Results: The findings indicated that MDR and non MDR isolates tended respectively to form weak and strong biofilms, formation. A high prevalence of fimH and PAP genes was found. In strains that were resistant to ampicillin, a significant correlate with biofilm producers was present. Another study showed that there was no significant reduction in biofilm in ampicillin sensitive strains. Antibiotic susceptibility testing showed that resistance among ESBLs producers was significantly higher than non-ESBLs producers. Moreover there was a significant correlation between ciprofloxacin and reduction in biofilm biomass.

Conclusion: All of these results confirm that acquisition of antimicrobial resistance could have a negative impact on the biofilm formation capacity among UPEC isolates. The prevalence of integrons and ESBLs are

remarkably associated with resistance to used antibiotics. These findings indicated that the significant between MDR phenotype and the potential for biofilm formation will lead to relapse of infection. Therefore, more investigations can be effective on the treatment of antibiotic resistance.

Keywords: Biofilm , Integron , UPEC , UTI , FimH

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Bioinformatic analysis of Amyloid-beta Precursor Protein (APP) and gene mutations related to Alzheimer's disease (Research Paper)

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Introduction: Alzheimer's disease is the most common form of dementia and is the only top 10 cause of death in the United States that lacks disease altering treatments It is a complex disorder with environmental and genetic components. There are two major types of Alzheimer's disease, early onset and the more common late onset. There are nearly 47 million people living with dementia worldwide, which is predicted to double every 20 years, increasing to more than 131 million by 2050. Alzheimer's disease (AD) is the best characterized among them, and it accounts for 50–60% of all dementia cases. This common neurodegenerative disease is clinically characterized by a progressive and gradual cognitive impairment, synapse loss, and substantial loss of neurons in later stages. The prevalence of dementia in the Western world in people over the age of 60 has been estimated to be greater than 5%, about two-thirds of which are due to Alzheimer's disease.

Methods: In this study, APP protein information was collected through NCBI, Uniprot and CATCH databases. Also, the mutations reported for APP gene of Alzheimer's disease were obtained through NCBI and Uniprot databases. Then, using SIFT and Polyphen site, the effects of these mutations on the disease were investigated separately, and finally, the common mutations were extracted and displayed in the form of statistically. Finally, we used NCBI to detect where the most regions had mutation.

Results: To advance our understanding of how APP and DR6 function together to initiate downstream signaling controlling axon pruning and synapse elimination, we determined the crystal structure of the APP/DR6 complex. The complex between the APP E2 domain and the ECD of DR6 was crystallized, and its structure was determined at 2.2 Å resolution, as described in the Materials and Methods. Consistent with previous studies, DR6 contains four CRD modules composed mostly of strands and loops of various lengths, with either two or three pairs of disulfide bonds stabilizing each CRD module. Based on SIFT, we found about 80 single nucleotide polymorphisms (SNPs) with a score between 0-0.04 that were deleterious and had pathogenicity

records in the UniProt database, and by analyzing the data by polyphen, the degree of damage in substitution We obtained amino acids with each other. The results showed that most of them were malignant and only 9 benign samples were found.

Conclusion: In this research, APP protein and gene mutations and their pathogenicity were investigated. APP, a well-investigated protein for AD development, is widely expressed across many tissues, including skeletal muscle. APP metabolism and its function in muscles are crucial for synapse development and maintenance at the NMJ. However, the molecular mechanisms that link muscular APP to the brain's pathology and function remain elusive. Identification of the role of APP in muscles will also establish the link between sarcopenia and neurodegenerative diseases. These may lead to insights into muscle brain crosstalk and suggest potential contributions to age-related degeneration.

Keywords: Amyloid-beta Precursor Protein (APP), Alzheimer's disease, Gene, mutation

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Bioinformatic analysis of COL7A1 gene mutations in Epidermolysis bullosa (EB) disease (Research Paper)

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Introduction: The epidermolysis bullosa (EB) family of inherited diseases is characterized by blistering in response to mechanical trauma. EB can produce painful wounds and erosions in skin, eyes, and mucosal tissues; can be mild or severe; and can heal with severe scarring or no scarring at all. Over 30 subtypes are recognized, grouped into four major categories, based predominantly on the plane of cleavage within the skin and reflecting the underlying molecular abnormality: EB simplex, junctional EB, dystrophic EB and Kindler EB. To date, pathogenetic mutations in 16 distinct genes have been implicated in EB, encoding proteins influencing cellular integrity and adhesion. COL7A1 is one of the genes that impact on this disease. This gene encodes the alpha chain of type VII collagen.

Methods: In this study, mutations reported for COL7A1 gene of EB disease were collected through UniProt and ClinVar databases. Then, by using SIFT and Polyphen-2 tools, the possible impact of an amino acid substitution on the structure and function of a human protein for epidermolysis bullosa disease was investigated separately, and common mutations were extracted and analyzed in the form of a statistical chart. Ultimately, we used NCBI to detect where the most regions had mutation.

Results: Based on VarSome, Most of the mutations that led to pathogenicity included Start loss, Nonsense, Frameshift and Splice junction loss. Based on SIFT tool, we found approximately 60 single nucleoutide polymorphism (SNP) with score between 0_0.03 that was deleterious and had pathogenicity records in UniProt and ClinVar databases and and by analyzing the data by polyphen we got the damage rate in replacing amino acids with each other. The results showed that most of them were malignant and only 2 benign samples were found. A common region for mutations affects the amino acid residues 2000-2835 that includes glycine rich domains and collagen triple helix repeat. Glycine and arginine were the most substituted amino acids.

Conclusion: In this research, we analyzed COL7A1 gene mutations and their pathogenicity. Mutations in arginine and glycine regions can cause different types of EB disease, which are very dangerous. dominant dystrophic epidermolysis bullosa usually involves glycine substitutions within the triple helix of COL7A1 although other missense mutations, deletions or splice-site mutations may underlie some cases. The recessive dystrophic epidermolysis bullosa mutations include nonsense mutations, splice site mutations, deletions or insertions, 'silent' glycine substitutions within the triple helix and non-glycine missense mutations within the triple helix domain. We can demonstrate the utility of bioinformatics in mutation detection and predict EB in a consanguineous family at risk for recurrence.

Keywords: COL7A1, Epidermolysis bullosa, mutation

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Bioinformatic analysis of GRIN2B gene and GluN2B protein mutations in autism spectrum disorder (ASD) disease (Research Paper)

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Introduction: Autism spectrum disorder (ASD) consists of a genetically heterogenous group of neurobehavioral disorders characterized by impairment in three behavioral domains including communication, social interaction, and stereotypic repetitive behaviors. Many of the genetic defects associated with ASD encode proteins that are relevant at the neuronal synapse or that are involved in activity-dependent changes in neurons, including regulatory proteins such as transcription factors. Transcriptional and splicing dysregulation or alterations in epigenetic mechanisms such as DNA methylation or histone acetylation and modification may play a role. GRIN2B is one of the genes that impact on this disease.The GRIN2B gene provides instructions for making a protein called GluN2B. This protein is found in nerve cells (neurons) in the brain, primarily during development before birth.

Methods: In this study, GluN2B protein information was collected through NCBI, Uniprot and PDB databases. Also, reported mutations for GRIN2B gene, which is effective in ASD, were obtained through NCBI and Uniprot databases. Then, by using SIFT and Polyphen sites, the effect of these mutations on the disease was investigated separately, and common mutations were extracted and analyzed in the form of a statistical chart. Eventually, we used NCBI to diagnosis where the most regions had mutation.

Results: According to PDB database, GluN2B receptor is a membrane protein and has 2 chains B and D and its sequence length is 862 amino acids. Based on SIFT, we found 24 single nucleoutide polymorphism (SNP) with score between 0_0.05 that was deleterious and had pathogenicity records in UniProt and ClinVar databases and and by analyzing the data by polyphen we got the damage rate in replacing amino acids witheachother. The results showed that most of them were malignant and only 4 benign samples were found.

Conclusion: In this research, we analyzed GRIN2B gene mutations and their pathogenicity. The detailed analysis of our study's findings highlighted the

significance of variation at the Thr685, Arg682, Asn615, and Ser526 positions involved in post-translational modifications directly or indirectly, which may be at the root of the destabilization of the GluN2B and, as a result, the occurrence of the disease. were identified as pathogenic, with the potential to inflict significant functional and stability impacts on the proteins.

Keywords: Autism spectrum disorder (ASD) disease, GRIN2B, GluN2B, Gene, mutation

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Bioinformatic analysis of three mutations G430D, L383R and R258H in the structure of fibrinogen β protein (Research Paper)

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Introduction: Congenital afibrinogenemia , a rare autosomal recessive disorder associated with a complete absence of fibrinogen in the bloodstream.Uncontrollable bleeding from the umbilical cord after birth is the most common symptom. Fibrinogen or coagulation factor 1 is a plasma-soluble glycoprotein, which is converted into fibrin strands in the coagulation cascade by thrombin. This protein consists of three chains Aα, β B and γ, each polypeptide is coded by a separate gene. Fibrinogen genes are clustered together on chromosome 4q28-31.In this study, the aim is to investigate the three missense mutations L383R in exon 7, G430D in exon 8, and R258H in exon 6 in the C-terminal part of fibrinogen β chain

Methods: In this article, Gene Runner, PAYMOL software and NCBI, SWISS-MODEL, PDB and UniProt databases are used to show the changes caused by this mutation on fibrinogen β protein.

Results: There are three nonsense mutations L383R in exon 7, G430D in exon 8, and R258H in exon 6 in the C-terminal part of fibrinogen β chain, which lead to decreased secretion of hexameric fibrinogen β complex

Conclusion: These mutations lead to a decrease in the secretion of hexameric fibrinogen β complex due to improper packing of β chains and improper folding of these chains.

Keywords: afibrinogenemia, fibrinogen β, nonsense mutation, glycoprotein

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Bioinformatic investigation of miR-128 miR-138 as genetic regulators in gastric cancer (Research Paper)

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Introduction: Gastric cancer is the second most frequent cause of cancer death worldwide, although much geographical variation in incidence exists. Prevention and personalised treatment are regarded as the best options to reduce gastric cancer mortality rates. Prevention strategies should be based on specific risk profiles, including Helicobacter pylori genotype, host gene polymorphisms, presence of precursor lesions, and environmental factors. Although adequate surgery remains the cornerstone of gastric cancer treatment, this single modality treatment seems to have reached its maximum achievable effect for local control and survival. Minimally invasive techniques can be used for treatment of early gastric cancers. Achievement of locoregional control for advanced disease remains very difficult. Therefore, the study of genetic and epigenetic regulatory factors and knowledge of these factors is important and can greatly help in the treatment of this disease.

Methods: First, we examined miR-128 and miR-138 in the comprehensive mirDB database and extracted all the information related to them and their target genes. Then, with the help of Kyoto gene encyclopedia (KEGG Pathway), we studied all the known metabolic pathways and roles of miR-128 and miR-138. Finally, with the help of COSMIC database, we were able to first confirm the role of these miRNAs in gastric cancer and identify all known mutations in them and their regulatory role.

Results: By doing all these studies, we found that miR-128 and miR-138 can be suitable candidates for molecular tests and we can count on their important and regulatory role in gastric cancer.

Conclusion: miR-128 and miR-138 have a positive regulatory role in the process of gastric cancer, and useful results can be obtained by studying them and their target genes.

Keywords: miR-128 , miR-138 , Gastric Cancer

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Bioinformatic investigation of miR-29 , miR-96 as genetic regulators in gastric cancer (Research Paper)

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Introduction: Background : Gastric cancer is one of the most common cancers and one of the most frequent causes of cancer-related deaths. The incidence, diagnostic studies, and therapeutic options have undergone important changes in the last decades, but the prognosis for gastric cancer patients remains poor, especially in more advanced stages. Surgery is the mainstay of treatment of this disease.

Methods: First, we examined miR-128 and miR-138 in the comprehensive mirDB database and extracted all the information related to them and their target genes. Then, with the help of Kyoto gene encyclopedia (KEGG Pathway), we studied all the known metabolic pathways and roles of miR-128 and miR-138. Finally, with the help of COSMIC database, we were able to first confirm the role of these miRNAs in gastric cancer and identify all known mutations in them and their regulatory role.

Results: After performing the necessary bioinformatics studies, the regulatory role of miR-29 and miR-96 and their importance in gastric cancer were confirmed. These results showed us that the molecular investigation of miR-29 and miR-96 can have positive results in the regulatory pathways and even the treatment process of gastric cancer.

Conclusion: miR-29 and miR-96 have a positive regulatory role in the process of gastric cancer, and useful results can be obtained by studying them and their target genes.

Keywords: miR-29 , miR-96 , Gastric Cancer

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Bioinformatic investigation of protein stability Mitogen activated protein kinase 3 (MAPK3) (Research Paper)

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Introduction: Mitogen-activated protein kinase3 (MAPK3) kinases are proteins that are specific for the amino acids serine, threonine, and tyrosine. MAPKs belong to the CMGC kinase group (CDK/MAPK/GSK3/CLK). MAPKs are involved in directing cellular responses to a diverse array of stimuli, such as mitogens, osmotic stress, heat shock, and proinflammatory cytokines. They regulate cell functions including proliferation, gene expression, differentiation, differentiation, cell survival and apoptosis. This study aims to analyze the bioinformatic characteristics of this disorder and evaluate the stability of this gene.

Methods: The characteristics of this gene were checked by GC counter and protparam sites.

Results: The characteristics of this gene were checked by GC counter and protparam sites. The results of the study showed that the percentage of GC was 35.5%. The theoretical pI of the investigated protein was 5.61. In this range, the target protein is precipitated. The higher the GC percentage of the examined protein, the more stable that protein is. Also, the instability index and aliphatic index for MAPK3 in the studied 36.92 and 89.89, respectively. Average GRAVY (hydrophobic property of protein) calculated for proteins is obtained by dividing the sum of hydropathy calculated for all amino acids in the protein by the total number of amino acids of that protein. In this research, Grand average of hydropathicity (GRAVY) -0.349 was obtained, which indicates the non-polarity of the investigated protein.

Conclusion: The results of bioinformatic analysis showed that this protein is the stable proteins and is able to maintain its structure completely at high temperatures.

Keywords: MAPK3 gene, stability, protparam

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Bioinformatic investigation of protein stability PEX6 (Research Paper)

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Introduction: Heimler syndrome is caused by mutations in the PEX6 gene. Heimler syndrome is a rare inherited systemic disorder that clinically overlaps relatively with Usher syndrome. Until today, our knowledge of Heimler's syndrome is very limited and in many cases the disease has been misdiagnosed or left undiagnosed. This study aims to analyze the bioinformatic characteristics of this disorder and evaluate the stability of this gene.

Methods: The characteristics of this gene were checked by GC counter and protparam sites.

Results: The results of the study showed that the percentage of GC was 44.8%. The theoretical pI of the investigated protein was 5.79. In this range, the target protein is precipitated. The higher the GC percentage of the examined protein, the more stable that protein is. Also, the instability index and aliphatic index for PEX6 in the studied 47.70 and 93.53, respectively. Average GRAVY (hydrophobic property of protein) calculated for proteins is obtained by dividing the sum of hydropathy calculated for all amino acids in the protein by the total number of amino acids of that protein. In this research, Grand average of hydropathicity (GRAVY) -0.196 was obtained, which indicates the non-polarity of the investigated protein.

Conclusion: The results of bioinformatic analysis showed that this protein is not among the stable proteins and is not able to maintain its structure completely at high temperatures.

Keywords: PEX6 gene, proptaram, gc counter

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Bioinformatic study of the anticancer potential of TFRA4 aptamer (Research Paper)

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Introduction: Introduction: Aptamers are short, single-stranded DNA or RNA (ssDNA or ssRNA) molecules that are used as drugs and drug carriers. DNA methylation is a post-replication epigenetic modification. DNA methyltransferases (DNMT) play a major role in regulating gene expression and producing and maintaining DNA methylation patterns. DNA methyltransferases are overexpressed in many types of tumors. For this reason, DNA methyltransferase inhibitor act on tumor cells as an anticancer agent. In this study, the anticancer potential of TFRA4 aptamer by inhibiting DNA methyltransferases was targeted.

Methods: Methods: First, we downloaded the appropriate protein code of DNA methyltransferases from the PDB website. DISCOVERY software was used to start the changes on the protein. Our protein code was 4wxx with a resolution of 2.62A. To make the necessary changes in this protein, the main chain of the protein was obtained and non-protein parts such as co-crystal and water molecules were deleted then the final protein in PDB format was saved. In the next step, to prepare the LP complex (ligand + protein) we used the docking approach. Finally, by the aptamer database site, we found complete information on the aptamer ligand.

Results: Results: TFRA4 aptamer with 14 nucleotides in length, molecular weight: 4338 g/mole, extinction coefficient: 146 L/(mole•cm), and GC content: 71.43% can bind to DNA methyltransferases. After complex analysis, we identified the Hbonds which including A:LYS697:NZ - :DT4:OP1, A:TYR976:OH - :DC12:OP1, A:ARG1311:NH1 - :DC9:OP2, A:ARG1311:NH1 - :DC9:OP2, A:GLN1340:NE2 - :DC9:OP1, A:GLN1340:NE2 - :DC9:O5' and DC5:N4 – A:GLU704:OE1

Conclusion: Conclusion: Finally, The TRF4 aptamer showed good inhibitory potential with a docking score of -230.37 and 7 Hbonds in the binding site of DNA methyltransferases.

Keywords: DNA methyltransferases, LP complex, Docking approach, TFRA4 aptamer, 4WXX

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Bioinformatics analysis of differential expression microRNAs and MALAT1's potential microRNA targets in breast cancer tissues (Research Paper)

Mobina Darabi,[1,*]

1. Tarbiat Modares

Introduction: MALAT1 is a controversial long-noncoding RNA with different and contrasting roles in breast cancer (BC). This lncRNA is involved in a pro-tumorigenic role in considerable solid tumors, including breast tumors and some lymphoid tumors, and on the contrary, plays an opposing role in the metastasis of breast cancer. Therefore, MALAT1 becomes a conceivable therapeutic target for breast cancer, so it is necessary to thoroughly investigate and comprehend the underlying reasons for the variations observed in MALAT1's role in tumorigenesis and the relationships between this lncRNA and its potential targets, such as microRNAs.

Methods: The RNAseq data of BC and healthy control (103 breast tumor tissue samples and 11 normal) were downloaded from the gene expression synthesis (GEO) GSE68085 (Krishnan P et al., 2016). Data were indexed by Bowtie and analyzed using the R package DESeq2. The transcriptomes of tumor tissue samples and healthy normal breast tissues were compared to identify microRNAs involved in breast cancer. Significant miRNAs (with high targeting scores) associated with long non-coding RNAs were searched through miRDB, starBase, and miRcode tools.

Results: We identified significant (padj <0.01) down-regulated expression of hsa-miR-1271-5p, hsa-miR-383-5p, and hsa-miR-4524a-5p, and up-regulated expression of hsa-miR-101-3p, hsa-miR-185-5p, hsa-miR-503-5p, hsa-miR-651-5p in tomur tissue cells. All of the mentioned microRNAs are potential targets for MALAT1. Three of them are up-regulated, and the others are down-regulated. So investigating the relationship between these miR and MALAT1 in different stages of tumors may help reveal the MALAT1 roles in BC.

Conclusion: All of the mentioned microRNAs are potential targets for MALAT1. Three of them are up-regulated, and the others are down-regulated. So investigating the relationship between these miR and MALAT1 in different stages of tumors may help reveal the MALAT1 roles in BC.

Keywords: MALAT1, breast cancer, miroRNA, noncoding RNA

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Bioinformatics Evaluation of signaling pathways targeting SNP related to the FTO in Obesity (Research Paper)

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Introduction: Obesity has become a serious global problem that still needs a solution. One of the factors that leads to Obesity is genetic predisposition. The identity and characteristics of the genes involved have not yet been Fully confirmed. Analyzing the genetic contribution to obesity is a major step towards the solution. Recent Studies have shown that obesity is largely influenced by heredity and created by the interactions between Several genes and environmental and behavioral factors.

Methods: The gene is located on chromosome 16 and its The product plays an important role in energy metabolism.By investigating the role of single nucleotide polymorphism sequences in the FTO gene in the occurrence of obesity and It is effect on the occurrence of mutated genotypes in people. A modified version of this gene is considered the Strongest genetic risk factor for obesity NCBI, KEGG and DAVID database sites were used to find Bioinformatics.

Results: Rs9939609 is predicted to This protein participates in the Absorption, according to the bioinformatics study in the present project and also according to the Previous contents in the FTO study. Accordingly, the aim of the present study was to investigate the Influence of the polymorphism on post-training changes of selected body mass and body composition Measurements, as well as with Biochemical parameters of energy metabolism.

Conclusion: The role of different pathways in genes and SNP obesity can be determined in each person’s functional metabolism.

Keywords: FTO,SNP,Obesity,Gene

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Bioinformatics-Driven Approaches for Precision Oncology: Revolutionizing Cancer Treatment (Review)

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Introduction: In the relentless battle against cancer, an innovative approach called precision oncology has emerged, marking a significant change in treatment strategies customized intricately to the unique genomic characteristics of each tumor. Leading this transformative movement is the interdisciplinary field of bioinformatics, which combines biology, computer science, and statistics, coordinating the analysis and understanding of extensive genomic datasets. By harnessing the potential of bioinformatics, researchers and medical experts smooth the way for personalized cancer care, revealing extraordinary opportunities for progress. This study aims to clarify some of crucial methods that collectively shed light on the path of cancer treatment evolution.

Methods: In this study, we have been focusing on more important bioinformatics approach related to precision oncology for cancer treatment. For this purpose, a total of 56 articles were collected.

Results: In the ever-evolving field of biomedical exploration, a range of innovative methods, including genomic profiling, functional annotation, pharmacogenomics, single-cell analysis, network biology, and drug repurposing, collaboratively drive humanity into an era characterized by the rise of personalized medicine. Genomic profiling, a detailed examination of an individual's genetic makeup, reveals profound insights into the complex mechanisms behind disease causality and progression. Concurrently, functional annotation decodes the intricate interactions and coordination among genes, unveiling the intricate ballet underlying cellular processes. Pharmacogenomics enables the customization of therapeutic approaches in alignment with genetic variations, mitigating the risk of adverse reactions and enhancing treatment effectiveness to unprecedented levels. Meanwhile, single-cell analysis, comparable to an exceptionally high-resolution microscope, delves into previously unexplored intricacies within cellular communities, exposing concealed aspects of disease onset and evolution, and ushering in a new era of precise prognostication. The frontiers of network

biology, a complex tapestry woven from molecular interactions, unveil the mysterious realm of intricate biological processes, providing insights into the key drivers of disease pathways and revealing new avenues for therapeutic intervention. In parallel, the strategy of drug repurposing expedites drug discovery by identifying fresh applications for existing pharmaceutical agents, bypassing the convoluted paths of drug development and rapidly translating concepts into revolutionary treatments.

Conclusion: These pioneering techniques synergistically catalyze a revolution across the medical landscape, fostering optimism for treatments that are targeted, effective, and finely tailored to the complexities of diverse ailments. As our understanding of biomedical knowledge continues to expand, interwoven with threads of genomics, computational analysis, and innovative methodologies, the prospect of truly personalized medicine becomes increasingly promising. The convergence of precision oncology and bioinformatics emerges as a forefront of this emerging healthcare era, poised to reshape the trajectory of cancer treatment and, by extension, offering a ray of hope across a spectrum of medical conditions.

Keywords: Personalized medicine; Bioinformatics; Cancer; Precision oncology

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Blood Glucose Fluctuations in Diabetic Patients Undergoing Elective Surgeries: A Comparative Analysis of Pre-Transfer and Post-Recovery Periods in the Operating Room (Research Paper)

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Introduction: Metabolic stress and insulin resistance are major surgical outcomes that result in postoperative hyperglycemia with increased mortality and morbidity in diabetic patients. Therefore, the aim of this study was to compare blood glucose changes in diabetic patients undergoing elective surgery immediately before being transferred to the operating room and after entering the recovery room.

Methods: This study was performed on 100 diabetic patients. After obtaining patient consent and demographic data, blood glucose levels were recorded before and after surgery. Chi-square and Mann-Whitney tests were used to compare the data.

Results: Mean blood glucose before surgery was 114.07 mg/dl and after surgery was 125.47 mg/dl (11.4 units increase), which was statistically significant (P <0.001) And this increase was significantly increased in patients over 60 years of age and under general anesthesia, but there was no significant difference in blood glucose, sex, BMI, history of addiction, blood pressure, or type of surgery.

Conclusion: Regarding the increase in post-operative blood glucose especially in the elderly and under general anesthesia and due to the increased complications of hyperglycemia in diabetic patients, evaluation of blood glucose before and after surgery can reduce complications in patients.

Keywords: Diabetes, Blood glucose, Surgery.

Botolinum Toxin for humans review article (Review)

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Introduction: Botulinum toxin or Botox is a neurotoxin produced by the bacterium Closterium Botolinum that grows and mostly reproduced in canned foods. There are 8 serotypes of this toxin, that the type A is used for cosmetic purposes. The toxin blocks the release of acetylcholine, causing local muscle paralysis. The toxin diffuses through tissues until it selectively and reversibly binds to the pre-synaptic end of the neuromuscular junction followed by attachment to specific protein membranes involved in acetylcholine secretion. The toxin Immediately inhibits the release of acetylcholine at the neuromuscular junction, resulting in reversible local relaxation of the muscles and a reduction in facial wrinkles/lines. This usually occurs from 24 hours after the toxin has been injected, to about 2 weeks after the procedure. This effect of the injection can be seen for about 3-6 months. Since the 1980s, they approved and started using Botox for the first time in the United States and then in 12 other countries. The experts came to the conclusion that although excessive amounts of this poison can be fatal for humans, its measured and permitted amounts can have many uses for them.

Methods: Currently, Botox is a leading non-surgical aesthetic treatment worldwide to reduce facial wrinkles, including glabellar lines(frowning lines between the two eyebrows), forehead lines and periorbital wrinkles. In order to investigate this issue in more detail, pay attention to this experiment: In an experiment in 2010, they examined the presence of lines and wrinkles on the faces of identical twin sisters and the effect of Botox injections. In this experiment, one of the sisters performed botox injections for 13 years and 2-3 times a year, and the other only 2 times a year for 7 years. The results were as follows: forehead lines and glabellar lines were not visible in the sister who had regular and longer treatment, but they were clearly visible in the other sister. Also, when smiling and even 7 months after the injection, less crow's feet wrinkles were seen in the person who had better treatment.No severe side effects were seen in any of them. In addition to beauty, Botox is also used to treat many diseases, like for people who have Eye problems such as uncontrollable blinking ,Severe muscle cramps (spasticity disease), Migraine and overactive bladder.

Results: As mentioned, Botox can be used to treat migraines. Of course, this injection will only be done for those who have headaches for more than 15 days a month and with the doctor's consultation. Here we examine a trial that shows how effective Botox is in treating migraines. In 2015, 106 patients—mostly women—who sought Botox treatment for both facial lines and headache disorders, or were considering Botox treatment for migraine headaches, were tested. Botox was injected in the glabellar, temporal lobe and forehead areas.

Conclusion: Although botox injection is suitable for most people without problems, it is not suitable for people with certain conditions. Therefore, it is necessary to consult with the doctor before the injection and provide him with your medical history so that you can refrain from Botox injection if necessary. Botox treatment is not recommended for It should also be noted that although the use of this treatment is allowed for most people, it is prohibited for some people. Now that you have obtained information about this treatment and some important issues, it is necessary to examine its short-term and long-term side effects.

Keywords: Botulinum Toxin,Botox,Cosmetic,Botox Injection,Facial wrinkles

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Breast cancer brain metastasis (BCBM): microRNA-Gene interaction analysis (Research Paper)

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Introduction: Breast cancer brain metastasis (BCBM) is a significant cause of brain metastases, particularly in patients with stage IV breast cancer. The incidence of brain metastases has been on the rise, with HER2-positive or triple-negative cancers associated with a higher risk. The understanding of the molecular mechanisms behind BCBM is still evolving, but specific gene mutations and expressional profiles in tumor cells have been identified. Treatment options for brain metastases include surgery, radiation therapy, and systemic therapy. MicroRNAs (miRNAs) play a crucial role in regulating cellular activities and are potential biomarkers for disease diagnosis and prognosis. Li et al. conducted a study analyzing mRNA and miRNA profiles in breast cancer specimens from patients with and without brain metastasis. The aim was to identify miRNAs associated with the pathways underlying BCBM. The study discovered several miRNAs linked to these pathways and further investigated their downstream molecular mechanisms through target genes. In this study, we first focused on identifying the most relevant microRNAs and their targets in breast cancer brain metastasis, and then investigated the downstream molecular mechanism using target genes.

Methods: In is study, the matrix data GSE100534 related to metastatic brain tissue derived from breast cancer with 35 samples downloaded from GEO database and were used to perform gene expression analysis by GEO2R. The level of p = 0.05 was used as the criterion for determining statistical significance and the threshold of |2| for Log 2 fold change was employed to identify differentially expressed genes (DEGs). MicroRNAs were predicted using the miRWalk database. Then, potential targets of the microRNAs were identified through the TargetScan, miRDB, and miRTarBase databases. The DAVID database was utilized to investigate the downstream regulatory pathways in KEGG. Target genes, were imported into Metascape for gene ontology and enrichment analysis. We also utilized Cytoscape software to conduct further analysis, using MCODE and CytoHubba plugins.

Results: 91 up-regulated genes and 25 down-regulated genes related to metastatic brain tissue derived from breast cancer were identified. For the up-regulated and down-regulated genes, 11 and 3 microRNAs were predicted respectively. The study found that hsa-miR-206, hsa-miR-7-5p, and hsa-miR-34a-5p microRNAs regulate down-regulated differentially expressed genes (DEGs). These microRNAs are enriched in the positive regulation of the miRNA transcription pathway. MCODE analysis identified a cluster of down-regulated target genes, including STX6, TFRC, and GJA1. Centrality analysis revealed that PDGFRA, CDK6, PIK3R3, MTMR9, TFRC, GJA1, KIF16B, ANKS1A, EGFR, and STX6 were the top hub genes based on the degree parameter. Dysregulation of GJA1 (Wu & Wang, 2019) and PDGFRA (Farooqi & Siddik, 2015) genes has been associated with various cancers, including breast cancer. The study suggests that the down-regulation of genes STX6, TFRC, and GJA1 through the activation of the positive regulation of miRNA transcription pathway leads to the activation of microRNAs, which promote brain metastasis in breast cancer. The study identified several microRNAs that are involved in the regulation of up-regulated differentially expressed genes (DEGs). These microRNAs are enriched in positive regulation of the miRNA metabolic process. Through MCODE analysis, a cluster of target genes was identified, including CCNT2, CCND1, E2F2, CCNY, CCND2, CCNE2, CCNJ, CDKN1A, and CDC25A. Centrality analysis highlighted hub genes such as CCND1, CSNK2A1, POLR2D, CCND2, CDKN1A, SMAD4, MYCN, and CBX5. The study suggests that the up-regulation of these genes leads to the activation of hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7d-5p, hsa-let-7e-5p, hsa-miR-98-5p, hsa-miR-23a-3p, hsa-miR-485-3p, hsa-miR-485-5p, hsa-miR-449a, and hsa-miR-449b-5p microRNAs, which in turn promote brain metastasis in breast cancer.

Conclusion: MicroRNA plays a crucial role in regulating gene expression and controlling cellular processes. Understanding the pathways affected by microRNA target genes is important for understanding their function and their association with diseases. In the case of brain metastasis, inhibiting the growth and invasion of primary tumors, such as breast cancer, could be a potential treatment approach. MicroRNAs and their targets can be used to suppress these pathways. Identifying target genes regulated by microRNAs can provide valuable insights into disease mechanisms and aid in the development of effective therapies.

Keywords: Breast cancer brain metastasis, microRNA, miR-Gene interaction analysis

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Breast cancer early diagnosis and detection with an application of magnetic resonance spectroscopy (Review)

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Introduction: Breast cancer is the most common cancer in women. Early diagnosis is critical for cancer treatment planning. Magnetic resonance imaging (MRI) has excellent contrast resolution, which can be of great importance for the detection of breast neoplasms. Multiparametric magnetic resonance-based techniques such as dynamic contrast-enhancement magnetic resonance (DCE-MRI), diffusion-weighted imaging (DWI), magnetic resonance spectroscopy (MRS), and magnetic resonance elastography (MRE) have the potential to organize patients according to pathology or their responses to treatment and improve clinical results. Magnetic resonance spectroscopy is an important tool that provides information about the biochemical composition and typifies the metabolic state of malignant, benign, and normal breast tissues. The purpose of this study was to evaluate the impact of magnetic resonance spectroscopy on the early detection of breast cancer.

Methods: This search was conducted in the Google Scholar database using the following keywords: “breast” and” cancer” detection” and” diagnosis” and “magnetic resonance spectroscopy” or “MRS”. We limited the publication period to 2022 to evaluate the most recent literature. We also used the PubMed database for additional literature searches. References to related articles were also included in this paper. After reading the abstracts, we manually selected relevant articles for this study.

Results: In the 4510 articles that we found by searching scientific websites, we limited our results to 27 papers based on the inclusion values. Magnetic resonance spectroscopy (MRS) is a noninvasive imaging modality often applied to evaluate the metabolic data inside a marked tissue by showing a spike in specific metabolites, such as total choline (tCho). MRS is often used to discover and detect other metabolites, such as lipids because aberrations in lipid metabolism are related to cancer growth. Elevated tCho levels have

been reported in malignant tumors, and combining lipid investigation with the tCho peak in MRS to detect breast cancer presented higher sensitivity compared to the situation where only one of them was deliberate.

Conclusion: Various studies have shown that MRS has sufficient sensitivity and accuracy to distinguish benign from malignant lesions. MRS performed at a higher field increases the sensitivity of tCho detection with better resolution. This study demonstrated the significant role of MRS in the detection and diagnosis of breast cancer lesions.

Keywords: breast cancer, magnetic resonance spectroscopy, detection

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Bridging Gaps in Multiple Sclerosis Care with Telehealth: Utilization Trends and Readiness Assessment (Research Paper)

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Introduction: Multiple Sclerosis (MS) is a complex neurological condition that often requires ongoing medical care and management. With the rapid expansion of telehealth services in recent years, there is a growing interest in its application to MS care. This article presents a comprehensive exploration of the readiness and utilization trends of telehealth solutions in the context of MS patient care.

Methods: In this cross-sectional research, we conducted a descriptive and analytical investigation involving individuals with MS who sought care at a referral MS clinic in Tehran. We administered a three-part questionnaire, encompassing demographic information, utilization of telehealth services by MS patients, and an assessment of their readiness to embrace telehealth services. The Technology Readiness Index (TRI 2.0) was employed, utilizing four dimensions: optimism, innovativeness, insecurity, and discomfort. Subsequently, we analyzed the collected data using both descriptive and inferential statistical methods. All data preprocessing and statistical analyses were carried out using SPSS version 26 and Microsoft Excel 2020.

Results: A total of 120 participants were involved in the study, with the majority being female (73%). According to the obtained results, 66% (120 out of 79) of the patients with MS have used remote health services at least once for managing their condition. Participants mentioned the following most common uses, in order: searching for information related to healthcare facilities and making appointments, searching for pharmacies for necessary medications, remote communication with their treating physician, and seeking information related to their disease. The average scores for willingness to

adopt telehealth services, optimism, innovativeness, insecurity, and discomfort were as follows: 3.266 (P<0.01), 3.633 (P<0.01), 3.273 (P<0.01), 3.031 (P>0.05), and 3.127 (P>0.05), respectively. Notably, there was no observed correlation between age, gender, marital status, educational attainment, employment status, disease type, disease duration, mobility, and the level of readiness to embrace telehealth among individuals with MS (P>0.05).

Conclusion: The readiness of patients with Multiple Sclerosis (MS) to utilize telehealth tools surpassed the average level significantly. In summary, these findings emphasize the increasing importance and acceptance of telehealth services within the MS patient community. While the results generally exhibit a positive trend, additional research and targeted interventions could prove advantageous in addressing potential concerns related to discomfort and insecurity, ultimately broadening the application of telehealth in the realm of MS care. Given the potential advantages of telehealth tools in delivering timely and high-quality information for self-managing their condition, it becomes crucial to introduce interventions aimed at bolstering patients' preparedness and eagerness to embrace these resources.

Keywords: Multiple sclerosis, Digital health, Telehealth, mHealth, Technology readiness

Bridging Genetic Variations from Pharmacogenomics to Improving Medications Efficiency in More Precise Parkinson's Disease Therapy (Review)

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Introduction: Parkinson's disease (PD) is a Neurodegenerative disorder, which characterized by a reduction of dopaminergic cells in the brain, located substantia nigra. Dopamine receptor agonists (DRAs) are a class of medications commonly prescribed for the management of PD symptoms. However, the response of DRAs can vary significantly among patients, and individual genetic factors play a crucial role in determining treatment outcomes. The pharmacogenomic considerations when prescribing DRAs for Parkinson's disease highlight the potential of personalized medicine in optimizing treatment outcomes and minimizing unwanted effects. By identifying genetic variations associated with DRA induction, personalized medicine approaches could be implemented in choosing better medications and dosage adjustments for individuals. Variations in critical genes that play a part in dopamine metabolism, such as receptor signaling and drug biotransformation, have been identified as potential precursors of DRAs in Parkinson's disease.

Methods: This comprehensive review aims to identify a holistic focus on gene-drug interactions, which result in diverse responses to one drug in different patients. Relevant databases, including Genecard, Scopus, and Web of Science, were searched by using keywords such as "pharmacogenomics," "dopamine receptor agonists," "Parkinson's disease," and "treatment." Relevant articles published between 2018 and 2023 were included in the study.

Results: Several studies have scoped on single nucleotide polymorphisms (SNPs) in genes such as DRD2, DRD3, and COMT, which have been associated with variations in DRA efficacy and tolerability. The DRD2 gene encodes dopamine D2 receptors, and SNPs in this gene have been associated with differences in DRA response. For instance, the TAQ1, a polymorphism (rs1800497) in the DRD2 gene, has been linked to a decrease in the D2 receptor expression in the striatum. Depending on allele expression,

they have been linked to variations in essential cognitive control functions. Similarly, SNPs in the DRD3 gene, which encodes dopamine D3 receptors, have also been implicated in DRA response. The Ser9Gly polymorphism (rs6280) in the DRD3 gene has been associated with a different response to DRAs such as Pramipexole. Additionally, Pramipexole must be administered at greater doses to PD patients with the Gly/Gly genotype to be clinically efficient compared to those with the Ser allele. The COMT gene encodes catechol-O-methyltransferase, an enzyme involved in dopamine metabolism. Variations in this gene, particularly the Val158Met polymorphism (rs4680), have been associated with differences in drug response. The rs4608 COMT gene polymorphism changes the motor response to entacapone, a COMT inhibitor. Individuals with higher COMT enzyme activity respond greater than those with lower COMT enzyme activity.

Conclusion: Pharmacogenetics considerations become crucial when optimizing the use of dopamine receptor agonists for Parkinson's disease; by incorporating pharmacogenetic information into care decisions, personalized therapy approaches can refine treatment outcomes. Nevertheless, several challenges must be addressed before pharmacogenetics can be fully embedded into clinical practice. Standardized testing protocols and guidelines for genetic testing are essential tools to ensure scalable and reliable results. Moreover, the viability of pharmacogenetic testing and the availability of alternative treatment options must be accounted for to ensure equitable access for all patients. Further research and clinical trials are needed to validate these findings and translate them into routine clinical practice. With continued advancements in pharmacogenetics, the future of personalized medicine for Parkinson's disease looks more promising.

Keywords: parkinson's disease, dopamine receptor agonists, pharmacogenomics, personalized medicine

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c-Myc decoy oligodeoxynucleotides-loaded polycationic nanoparticles inhibit cell growth and induce apoptosis in NTERA-2 cells (Research Paper)

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Introduction: An increase in cancer stem cell (CSC) populations and their resistance to common treatments could be a result of dysregulation of c-Myc in certain cancer cells. In the present study, we investigated anticancer effects of c-Myc decoy ODNs loaded in poly (methacrylic acid-co-diallyl dimethyl ammonium chloride) (PMA-DDA)-coated silica nanoparticles as carriers on NTERA-2 cancer cells.

Methods: The physicochemical characteristics of the synthesized nanocomposites (SiO2@PMA-DDA-Dec) were analyzed using FE-SEM, DLS, FT-IR, and Zetasizer techniques. UV-Vis spectrophotometer was applied to analyze the release pattern of decoy ODNs from the nanocomposite. Furthermore, uptake, cell viability, apoptosis, and cell cycle assays were used to investigate the anticancer effects of nanocomposites loaded with c-Myc decoy ODNs on NTERA-2 cancer cells.

Results: The results of physicochemical analytics demonstrated that SiO2@PMA-DDA-Dec nanocomposites were successfully synthesized. The prepared nanocomposites were taken up by NTERA-2 cells with high efficiency, and could effectively inhibit cell growth and increase apoptosis rate in the treated cells compared to the control group. Moreover, SiO2@PMA-DDA nanocomposites loaded with c-Myc decoy ODNs induced cell cycle arrest at G0/G1 phase in the treated cells.

Conclusion: The conclusion drawn from this study is that c-Myc decoy ODN-loaded SiO2@PMA-DDA nanocomposites can effectively inhibit cell growth and induce apoptosis in NTERA-2 cancer cells. Moreover, given that a metal core is incorporated into this synthetic nanocomposite, it could potentially be used as a radiosensitizer in conjunction with X-irradiation as part of a decoy-radiotherapy combination therapy in future investigations.

Keywords: c-Myc transcription factor, decoy ODNs, polycationic nanoparticle, NTERA-2 cell line.

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Ca19Zn2(PO4)14 Nanoparticles: Synthesis, characterization and its effect on the colonization of Streptococcus mutans on tooth surface (Research Paper)

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Introduction: BACKGROUND AND ABJECTIVE The main cause of tooth decay is the biofilm formation of Streptococcus mutans. This study aimed to investigate the effect of the zinc oxide nanoparticles (ZnO NPs), hydroxyapatite nanoparticles (Ca10(PO4)6(OH)2) (HAP NPs), zinc oxide/hydroxyapatite nanocomposites (ZnO/HAP NCs), and Zn substituted hydroxyapatite nanoparticles (Ca19Zn2(PO4)14 NPs) on the growth and biofilm formation, bacterial adherence, and the expression of ftf and gtfC genes in Streptococcus mutans.

Methods: MATERIALS AND METHODS The nanostructures were prepared via simple and fast co-precipitation route. Twelve isolates of Streptococcus mutans collected from children with dental caries referred to the dental clinic of Kashan University of Medical Sciences. All S. mutans isolates were susceptible to Ampicillin.

Results: RESULTS AND DISCUSSION The mean MIC for ZnO NPs, HAP NPs, Ca19Zn2(PO4)14, and ZnO/HAP NCs were 118, 260, 70.6, and 994 mg/mL, respectively. All prepared nanostructures significantly reduced biofilm formation at MIC and sub-MIC concentrations ($p < 0.01$). In biofilm and cell culture treated with nanoparticles, the expression of ftf and gtfC genes decreased. Results were shown that IC50 for the Ca19Zn2(PO4)14 was 8.5, and for non-toxic concentration, was 0.065 mg/mL. The attachment rate to the denture surface and HGF1 cell line treated with the Ca19Zn2(PO4)14 NPs has decreased.

Conclusion: CONCLUSION The results showed that the Ca19Zn2(PO4)14 NPs has a better effect than the ZnO/HAP NCs. It can therefore be used as a coating on dental surfaces. Investigation of Ca19Zn2(PO4)14 NPs form for covering dental teeth surface recommended in future study.

Keywords: Hydroxyapatite ,Nanocomposites ,Biofilm ,MIC ,Dental

Can Diabetes Mellitus affect Candida species diversity? A narrative review (Review)

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Introduction: Diabetes is a pervasive chronic metabolic disorder that afflicts millions globally. In addition to the primary complications associated to diabetes, such as cardiovascular disease and neuropathy, recent research has unveiled a potential connection between diabetes and Candida infections. Candida, a genus of opportunistic fungi, is ubiquitously distributed within the human body, colonizing sites including the gastrointestinal tract, skin, and mucous membranes. This narrative review aims to meticulously scrutinize the intricate relationship between distinct Candida species and diabetes, elucidating the underlying mechanisms and potential therapeutic implications.

Methods: This comprehensive literature search was meticulously executed, encompassing various databases, notably PubMed, Scopus, and Google Scholar. The search parameters incorporated keywords such as "Candida," "diabetes," "Candida and diabetes," "Candida species," and "diabetes complications." This review encompasses pertinent articles published in the English language over the preceding two decades.

Results: 1. Species-Specific Prevalence: Research consistently unveils Candida albicans as the predominant species in both diabetic and non-diabetic populations. However, individuals with diabetes exhibit heightened susceptibility to other Candida species, prominently Candida glabrata and Candida tropicalis, which are relatively infrequent in healthy cohorts. 2. Glycemic Control and Candida: Findings substantiate a direct correlation between glycemic control and Candida infections. Inadequate diabetes management, marked by elevated blood glucose levels, significantly augments the incidence of Candida infections. This underscores the imperative nature of maintaining optimal blood glucose levels to ameliorate Candida-related complications in diabetes. 3. Biofilm Formation: Research convincingly demonstrates that Candida species, particularly Candida albicans, intricately fashion biofilms on mucosal surfaces in diabetic

individuals. These biofilms exhibit remarkable resistance to therapeutic interventions, engendering persistent and recurrent infections, thereby complicating diabetes management. 4. Species-Specific Antifungal Resistance: Studies meticulously delineate variations in antifungal susceptibility among disparate Candida species. Notably, Candida glabrata frequently manifests reduced responsiveness to commonplace antifungal agents, posing formidable challenges in the treatment of diabetic patients. 5. Immune Response: Investigations unveil compromised immune responses within diabetic individuals, characterized by impaired neutrophil and macrophage function. This compromised immune defense substantially heightens susceptibility to Candida infections, particularly in instances of uncontrolled diabetes.

Conclusion: The relationships between Candida species and diabetes are multifaceted and intricate. Through the application of advanced molecular methodologies and the inclusion of diverse patient cohorts, researchers have gleaned critical insights. These findings underscore the paramount importance of glycemic control, the prevalence of specific Candida species, the pivotal role of biofilm formation, and the variances in antifungal resistance. Comprehending these intricate relationships is pivotal for the development of tailored treatment strategies and the enhancement of outcomes for diabetic individuals. Ongoing research in this realm promises to further refine our understanding of these intricate interactions.

Keywords: Diabetes , Candidiasis , Diabetes Mellitus

Can omega-3 polyunsaturated fatty acids affect health outcomes in women with breast cancer? A systematic review (Review)

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Introduction: Breast cancer (BC) is the most prevalent cancer in women and ranks fifth in cancer-related deaths. In 2020, approximately 2.3 million new BC cases and 658,000 BC-related deaths were reported. BC is a complex disease influenced by several factors including genetics, family history of BC, previous ovarian cancer, lifestyle, marital status, and late menopause. Recent preclinical and clinical studies have demonstrated that omega-3 polyunsaturated fatty acids (ω-3 PUFA) are an effective adjunctive therapeutic strategy for the treatment of breast cancer. The administration of ω-3 PUFAs, specifically eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), has been found to mitigate the side effects of chemotherapy and enhance progression-free survival as well as overall survival in breast cancer patients. However, the findings are conflicting and appear inconsistent.

Methods: A search was conducted in MEDLINE (PubMed), Scopus, and Web of Science databases up to August 2023. Randomized clinical trials (RCTs) reporting the association between omega-3 fatty acid intake and health outcomes in women with breast cancer were included.

Results: After the application of inclusion/exclusion criteria, a final sample of 11 articles were included for this review. TG, CRP, total leukocytes, lymphocytes, leptin, adiponectin, and omega-6:omega-3 ratio decreased in the intervention group compared to the placebo counterparts. However, there was no difference observed in the serum lipid profile and serum albumin compared to the placebo group.

Conclusion: In conclusion, supplementation of omega-3 polyunsaturated fatty acids (ω-3 PUFA) may have a positive impact on the prevention and treatment of breast cancer, leading to improvements in physical and mental health as well as reductions in inflammation and metabolic issues. Further

research regarding the effect of omega-3 FAs on health outcomes in BC patients under chemotherapy is suggested.

Keywords: Breast cancer, DHA, EPA

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Can Synbiotics Affect Health Outcomes in Patients with NAFLD? A Systematic Review (Review)

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Introduction: Alterations in the gut microbiota, due to environmental and genetic factors, can disrupt intestinal homeostasis. This disruption can lead to a deregulation of the host's metabolism and immune system, thereby increasing the risk factors for the onset and exacerbation of non-alcoholic fatty liver disease (NAFLD). The administration of synbiotics has been viewed as a potential and promising approach to modulate the gut microbiota and yield beneficial outcomes in patients with hepatic disorders. This review sought to assess the efficacy of synbiotics in patients diagnosed with NAFLD.

Methods: PubMed, Web of Science, Embace and Cochrane Library were systematically searched for trials on the use of synbiotic supplements in patients with NAFLD. RCTs investigating the effects of synbiotic supplementation in patients diagnosed with NAFLD were included.

Results: Of 375 identified articles, 10 RCTs were eligible and finally included in this study. ALT and AST were reported in 9 studies. The significant difference suggest that synbiotic supplementation can significantly lower ALT and AST levels in these patients. Similarly, GGT, TC and CAP were significantly decreased after supplementation. However, the results show no significant difference in TG, IR, and insulin levels.

Conclusion: In conclusion, our study found that symbiotic supplementation significantly improved liver function, adjusted lipid metabolism, and delayed progression of NAFLD. Further well-designed studies with a larger sample size are recommended.

Keywords: NAFLD, Synbiotics

Cancer Immunotherapy using CRISPR/Cas9 system; a powerful tool (Review)

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Introduction: The emergence of CRISPR-Cas9 genome editing tool has revolutionized the field of biotechnology, offering unparalleled potential in various disciplines, including cancer immunotherapy. This article provides an overview of how CRISPR-Cas9 is being utilized to enhance the effectiveness of cancer immunotherapy. Cancer immunotherapy aims to harness the body's immune system to recognize and eliminate cancer cells. However, numerous challenges, including tumor heterogeneity and immune evasion mechanisms adopted by cancer cells, limit the efficacy of current immunotherapeutic approaches. CRISPR-Cas9 presents a powerful tool to overcome these challenges by enabling precise and targeted modifications in the genome of immune cells and tumor cells.

Methods: Engineering Immune Cells using CRISPR-Cas9 One of the key applications of CRISPR-Cas9 in cancer immunotherapy involves editing immune cells, such as T cells, to enhance their anti-tumor activity. By manipulating genes encoding immune checkpoints, co-stimulatory molecules, or chimeric antigen receptors (CARs), scientists can optimize T cell function and response against cancer cells. This approach has shown promising results, with engineered T cells exhibiting enhanced tumor recognition and killing abilities in preclinical and clinical studies. This approach has also been used to modify immune cells to target solid tumors, which are often resistant to traditional treatments. CART cell therapy involves genetically modifying a patient's T-cells to express a chimeric antigen receptor (CAR) that can recognize and bind to specific proteins on cancer cells. The CAR is composed of an extracellular domain that recognizes the target protein, a transmembrane domain, and an intracellular signaling domain that activates the T-cell when the CAR binds to the target protein. Once the T-cells are modified, they are expanded in the laboratory and infused back into the patient. The CART cells then migrate to the site of the cancer and bind to the target protein on the cancer cells, leading to their destruction. Modifying Tumor Cells with CRISPR-Cas9 Another application of CRISPR-Cas9 in cancer immunotherapy is the modification of cancer cells themselves.

Through gene editing, researchers can disrupt genes responsible for immune evasion mechanisms or induce the expression of immune-stimulatory molecules on tumor cells. This modification induces tumor vulnerability to immune attack and stimulates anti-tumor immune responses, leading to improved therapeutic outcomes. Targeting Key Genes Involved in Immune Regulation CRISPR-Cas9 can be utilized to target genes involved in immune regulation, such as ytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) or Transforming growth factor beta (TGF-β). By disrupting these genes, the immunosuppressive signals in the tumor microenvironment can be attenuated, leading to enhanced anti-tumor immune responses.

Results: Development of personalized cancer vaccines with CRISPR-Cas9 technology Moreover, CRISPR-Cas9 technology is facilitating the development of personalized cancer vaccines. By introducing tumor-specific antigens into immune cells, scientists can boost the immune system's ability to recognize and eliminate cancer cells. CRISPR-Cas9 allows precise editing of antigens, ensuring optimal immunogenicity and safety of personalized vaccines. Challenges and Future Directions Despite its immense potential, challenges and ethical considerations surround the application of CRISPR-Cas9 in cancer immunotherapy. Off-target effects and long-term safety concerns require careful monitoring and testing. To reduce off-target cleavage, the guide RNA should be designed with high sequence homology to the target gene. In addition, Cas9-crRNA should be delivered by viral vector or plasmid, which can minimize the potential mutations caused in guide RNA synthesis. Recently, engineered or natural Cas9 ortholog proteins have been developed to improve its specificity and efficiency. Additionally, Researchers must ensure that the modified immune cells do not cause harm to the patient, and there is also a risk of unintended consequences from modifying genes. Recently, Professor Zhang and colleagues observed a system similar to CRISPR in eukaryotic cells, which was named OMEGA. The most interesting point after this discovery will be that maybe in the near future for human genetic manipulation, we only need to deliver the sgRNA sequence to the target cell and the rest of the protein components will be supplied from within the cell itself.

Conclusion: In conclusion, the application of CRISPR-Cas9 genome editing tool in cancer immunotherapy holds immense promise for revolutionizing cancer treatment. Through precise genetic modifications of immune cells and cancer cells, the efficacy and specificity of current immunotherapeutic approaches can be improved. Continued research and innovation in this field

will contribute to the development of safe and effective therapies, bringing us closer to defeating cancer.

Keywords: CRISPR/Cas9, Genome Editing, Cancer Immunotherapy, Cancer Treatment, Immune Response

Cancer Stem Cells and Therapeutic Implications Review Article (Review)

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Introduction: Cancer, a complex and multifaceted disease, has been the subject of extensive research and investigation for centuries. Over the years, our understanding of cancer has evolved significantly, leading to breakthroughs in diagnosis, treatment, and prevention. One area of particular interest is the concept of cancer stem cells (CSCs), which has gained prominence in recent decades. The concept of stemness in cancer can be traced back to the mid-19th century when the first theory on the embryonic origin of cancer was formulated. It was not until the mid-20th century that significant progress was made in understanding cancer stem cells through studies on embryonal carcinoma cells. These early studies laid the foundation for the current cancer stem cell theory, which postulates that tumor growth is supported by a small fraction of tumoral cells that possess stem-like properties. In recent years, there has been a growing body of evidence challenging and expanding our understanding of CSCs. It is now recognized that intratumor heterogeneity plays a crucial role in cancer progression and treatment response. Intratumor heterogeneity refers to the presence of diverse subpopulations of cancer cells within a tumor, each with distinct genotypes and phenotypes. This heterogeneity arises from genetic mutations, epigenetic modifications, and interactions with the tumor microenvironment. Cancer stem cells are a subset of cells within a tumor that exhibit self-renewal capacity and the ability to differentiate into various cell types found within the tumor. These cells are thought to be responsible for tumor initiation, maintenance, and resistance to therapy. CSCs have been identified in various types of cancer, including breast cancer, leukemia, brain tumors, and colorectal cancer, among others. Understanding the mechanisms underlying intratumor heterogeneity and CSC biology is crucial for the development of effective cancer therapies. Recent studies have highlighted the role of epigenetic mechanisms in driving phenotypic differences between CSCs and non-CSCs. Epigenetic changes, such as DNA methylation and histone modifications, can alter gene expression patterns and contribute to the maintenance of CSC properties.

Methods: The discovery of CSC-specific biomarkers has also opened up new avenues for targeted therapies. By identifying and targeting specific surface markers or signaling pathways expressed by CSCs, researchers aim to selectively eliminate these cells and disrupt tumor growth. Additionally, novel therapeutic strategies have emerged that focus on modulating the tumor microenvironment to inhibit CSC activity and sensitize tumors to conventional treatments. Immunotherapy, which harnesses the body's immune system to recognize and destroy cancer cells, has shown promising results in targeting CSCs. By stimulating an immune response against CSC-specific antigens, immunotherapy holds the potential to eradicate CSCs and prevent tumor recurrence. Furthermore, advancements in gene therapy techniques offer the possibility of directly targeting CSCs by delivering therapeutic genes or RNA molecules specifically to these cells. Combination therapies that target both CSCs and non-CSCs have also gained attention as a strategy to overcome treatment resistance and improve patient outcomes. By simultaneously targeting multiple pathways involved in tumor growth and maintenance, these combination approaches aim to achieve more comprehensive and durable responses.

Results: Combination therapies that target both CSCs and non-CSCs have also gained attention as a strategy to overcome treatment resistance and improve patient outcomes. By simultaneously targeting multiple pathways involved in tumor growth and maintenance, these combination approaches aim to achieve more comprehensive and durable responses. In conclusion, the study of cancer stem cells and intratumor heterogeneity has revolutionized our understanding of cancer biology and treatment. The recognition that CSCs play a crucial role in tumor initiation, maintenance, and therapy resistance has opened up new avenues for targeted therapies.

Conclusion: Advances in epigenetics, biomarker discovery, immunotherapy, gene therapy, and combination therapies hold great promise for improving patient outcomes and transforming cancer treatment into a more personalized and effective approach. Continued research into CSC biology and intratumor heterogeneity will undoubtedly lead to further breakthroughs in our fight against cancer.

Keywords: cancer stem cells, stem cell therapy, resistance to therapy, tumor heterogeneity

Cancer vaccines based on self-replicating RNA (Review)

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Introduction: Introduction: Therapeutic vaccines for cancer that specifically target certain genes within the immune system employ preexisting platforms for their delivery. One prominent platform utilized is messenger RNA (mRNA), which has demonstrated success in SARS-CoV2 vaccines

Methods: Methoda: A review of articles from two databases, PubMed and Scopus, was conducted, and by considering articles with a high impact factor, the most frequently used articles were extracted. The content is presented in three parts, including the AVX-701 engineered vaccine, the PSMA-carrying vaccine, and the HER2 anti-cancer vaccine.

Results: Results:These vectors are derived from positive strand RNA viruses. Within these vectors, the coding genes of the structural genes are substituted for the intended application. In order to generate virus particles possessing only a single replication capacity (VRPs), structural providers are employed within a distinct and specialized vector. The srRNA vectors that have reached the clinical stage are derived from alphaviruses such as Venezuelan equine encephalitis (VEE) and African SFV. These carriers harbor codes that correspond to specific tumor antigens. Among these genetic codes are those for carcinoembryonic antigen (CEA), human epidermal growth factor receptor number 2 (HER2), prostate-specific membrane antigen (PSMA), as well as the antigens produced by the human papilloma virus (HPV), namely E6 and E7. The primary side effects associated with this particular type of vaccine primarily consist of grade 1 toxicity and milder reactions at the injection site. This article presents a comprehensive review of the clinical responses to this type of vaccine and provides relevant information pertaining to the safety of these vaccines.

Conclusion: Clinical trials of self-replicating RNA (srRNA) vaccines using virus-mimicking particles show a favorable safety profile and minimal toxicity. Despite the emergence of neutralizing antibodies specific for similar virus particles, a high level of antigen-specific T and B cell responses is induced. Fully synthetic srRNAs show promise in enhancing immune responses when used as part of primary boosting strategies. The absence of the virus shell in these nanoparticles reduces the anti-carrier immunity and allows for insidious

dosingand facilitates the inclusion of several larger genes of interest into the vector.Furthermore, the experience gained from the development of srRNA and their delivery vehicles for infectious diseases promises significant potential for the future development of srRNA platforms for the treatment of malignancies.

Keywords: Keywords: srRNA vaccine, VRP, PSMA, HER2, cancer

CAR T-Cell Therapy for Non-B-cell acute leukemia (Review)

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Introduction: CAR T-Cell Therapy for Non-B-cell acute leukemia Introduction: T-cell acute lymphoblastic leukemia (T-ALL) and acute myeloid leukemia (AML) are both included in the category of non-B-cell acute leukemia. AML is a type of hematological cancer that develops from the aberrant clonal expansion of primary myeloid cells. The malignant transformation of immature T-cell progenitors causes T-ALL, a very invasive type of hematological cancer. The therapeutic efficacy of available therapies for refractory or relapsed (R/R) non-B-cell acute leukemia is currently constrained. Given its encouraging outcomes in the treatment of B-cell acute lymphoblastic leukemia (B-ALL), chimeric antigen receptor (CAR)-T cell therapy may be a potential strategy to treat non-B-cell acute leukemia in such circumstances. We list the characteristics of non-B-cell acute leukemia and the effectiveness of CAR-T for treating it in this review. Benefits of CAR-T therapy When compared to TCRs, CARs are independent of the major histocompatibility complex (MHC) and can detect specific antigens presence on the surface of cells. Because they are MHC independent, CAR-T cells are better suited for the treatment of tumors. By identifying tumor-specific antigens (TSA) on the surface of tumor cells, CAR-T cells destroy cancerous cells while causing the least amount of damage to healthy tissues. CAR-T therapy challenges for non-B-cell acute leukemia Fratricide, malignant contamination, T-cell aplasia for T-ALL, antigen heterogeneity, and immunosuppressive environments are only a few of the particular difficulties facing the development of CAR-T treatment for non-B-cell acute leukemia. CAR-T therapy's antigen targets for treating T-ALL About 80%–95% of T-ALL or T lymphoblastic lymphoma (TLL) display CD5, a surface marker of T-cell malignancies. Normal expression of CD5 on mature peripheral blood T cells, thymocytes, and certain B-cell lymphocytes in healthy tissues promotes CAR-T cell fratricide. For CD5+ hematological malignancies, CD5 is a hopeful target. All mature T-cells largely display the pan-T-cell surface antigen CD3, but due to the total fratricide of CAR-T cells, the development of CAR-T targeting CD3 is restricted in the early stages. Clinical use of CARs targeting CD3 is constrained due to the fact that T-ALL and TLL cells produced from patients often display cytoplasmic CD3 (cCD3) rather than membrane CD3 (mCD3). Over 95% of ALL, 30% of AML, and some lymphomas express CD7, a member of the Ig superfamily. Initially, CAR-T cells directed against CD7

displayed total fratricide and could not be used; however, in recent clinical trials, CD7 CAR have demonstrated satisfactory efficacy and safety. Fratricide can now be eliminated using gene editing technologies such as CRISPR-Cas9, TALEN, or PEBL. Most TLLs and certain T-ALLs express CD4, and this expression is only found in the hematopoietic compartment. As the CAR's target, it may lessen the adverse effects on tissues other than hematological ones. However, the survival of CD4 CAR T cells after the excision of tumor cells can result in the aplasia of CD4 positive T cells and an illness similar to HIV/AIDS. CAR-T therapy's antigen targets in AML CD123, which is expressed at low levels in early hematopoietic cells such hematopoietic stem/progenitor cells (HSPCs), is one potential target for AML. Because of CD123 ability that can discriminate HSC from leukemia stem cells(LSCs), to eradicate LSCs and maintain normal HSC, TALEN gene-editing technology was employed to create a TCRαβ negative allogeneic CD123 CAR (UCART123), which eradicate primary AML. The anti-tumor efficacy, proliferation, and perseverance of CD33 CAR-T cells may be impacted by various costimulators, distinct generation CAR constructions, and PI3K inhibitors. CD33 CAR demonstrated effective anti-AML activity in vitro. More than 80% of LSCs and AML blasts express C-type lectin-like molecule-1 (CLL-1). In pre-clinical studies, CLL1 CAR shown encouraging anti-tumor effectiveness, and in AML patients, it demonstrated anti-AML efficacy. Most AML blasts and AML stem/progenitor cells express CD70, a tumor necrosis factor (TNF) receptor ligand. In the clinical trial, more research on the CD70 CAR's efficacy and safety in patients is required.

Methods: this is a review article and doesn't have this part

Results: this is a review article and doesn't have this part

Conclusion: Conclusion T-ALL and AML are types of leukemia that have more complicated morphological characteristics than B-ALL and are linked to a poor prognosis. T-ALL and AML also have fewer therapy choices available after recurrence or refractory. Given the enormous success of CAR-T cell therapy in B-cell malignancies, adopting a similar strategy for non-B-cell acute leukemia seems to be a potential path for the creation of better therapies.

Keywords: T-ALL, AML, CAR T-Cell Therapy, leukemia

Carbapenem resistant pathogens: a major challenge to public health (Review)

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Introduction: Among various beta-lactam antibiotics, carbapenems are highly effective antimicrobial agents for treating important hospital-acquired infections. Carbapenems exert their bactericidal activity by binding to penicillin-binding proteins (PBPs), membrane-associated proteins responsible for the synthesis of peptidoglycan in the cell wall of bacteria. Due to their broad spectrum of activity against both gram-positive and gram-negative bacteria, stability against most beta-lactamases, good safety profile, and appropriate tolerance, carbapenems are commonly considered as the last and most reliable antibiotic option for the treatment of critically ill patients and serious infections caused by multidrug-resistant (MDR) organisms. Excessive use of carbapenems in many countries has given rise to carbapenem resistance, especially among gram-negative bacteria. This article examines the importance of carbapenem-resistant pathogens as a major public health problem.

Methods: In this review, we searched and summarized recently published studies related to carbapenem resistance in Google Scholar, PubMed, Scopus, … databases. The search was performed using keywords such as carbapenem, carbapenem resistance, carbapenemase, and public health.

Results: Resistance to carbapenem antibiotics can be caused by several mechanisms such as carbapenemase production, porin mutation, or efflux pump upregulation . However, production of carbapenemases is the main mechanism of carbapenem resistance and is a major challenge because these enzymes hydrolyze almost all beta-lactams and are encoded by genes

that can be transferred horizontally by mobile genetic elements such as: plasmids, integrons, and transposons. In addition, carbapenemase-producing bacteria are usually resistant to other classes of antibiotics, including aminoglycosides and fluoroquinolones. The KPC, VIM, IMP, NDM, and OXA-48 types are considered to be the most potent carbapenemases due to their strong ability to hydrolyze carbapenems and widespread distribution. However, with the rise of international travel and the growth of medical tourism, the association between a particular resistance mechanism and a specific region or country can change. Some human-related factors such as irrational antibiotic prescription, uncontrolled public access to antibiotics, lack of appropriate infection control measures in healthcare settings and the use of antibiotics as growth promoters in livestock and poultry have played an important role in the emergence and spread of carbapenem resistance. In addition, prolonged use of metronidazole and imipenem drugs, prolonged hospital stays, and the presence of biliary drainage catheters have been identified as effective factors for the acquisition of carbapenem resistance. The rapid spread of antimicrobial resistance is a concerning issue. If resistance continues at this rate, untreatable infections will appear on a large scale, in some cases, the world may experience the uncomfortable pre-antibiotic era. The emergence of carbapenem-resistant pathogens (CRPs), including carbapenem-resistant Enterobacteriaceae (CRE), carbapenem-resistant Acinetobacter baumannii (CRAB), and carbapenem-resistant Pseudomonas aeruginosa (CRPA), is a significant and concerning global threat. Because of the reduction of treatment options, the mortality following CRP infection is up to 50%. Due to the importance of this issue, World Health Organization has classified CRPs as critical priority pathogens for the discovery, research and development of new antibiotics. Although many new treatment options, such as carbapenemase inhibitor compounds, are in the process, none of them provide a complete solution for addressing this concerning threat.

Conclusion: The rapid spread of carbapenem resistance in the community is a growing and emerging threat to public health. Despite some efforts made in this field, the production of new and effective antibiotics is a time-consuming and expensive process and is not profitable compared to the production of drugs in other medical fields, so it seems that finding a definitive and efficient solution to this problem is complicated and difficult. Therefore, in the absence of a dependable substitute to carbapenems, rational use of antibiotics in humans and animals, implementation of strict infection control measures, and active surveillance for the presence of carbapenemase-encoding genes are among the most crucial actions that can be taken.

Keywords: Carbapenem Resistance, Carbapenemase, Public health

Carbon nanotubes in treatment and drug delivery review article (Review)

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Introduction: Carbon nanotube(CNT)has a wide rang of applications in clouding physics,chemistry and materials sciences(CNT)were discovered in 1991 by lijima.CNTs with attractive physico chemical characteristics such as high surface area,mechanical strength,functionality,and electrical/thermal conductivity have been widely studied in different fields of science. CNTs have been synthesized using various natural hydrocarbon precursors,including plant extracts essential oils,biodiesel,milk honey,and eggs,among others. Researchers should embrace the usage of natural and renewable precursors as well as greener methods to produce various types of CNTs in large quantities with the advantages of cost_effectiveness and environ mentally benign features.CNTs it be longs to the fullerenes family and is categorized in to single_walled carbon Nanotubes(SWNTs)or multi walled carbon nanotubes(MWNTs).Single_walled(SW)and multi_walled(MW)carbon nanotubes(CNTs)Ara two main categories of CNTs,based on the number of graphene sheets comprising the cylindrical tube.These cylindrical nanostuctures can be employed for various pharmaceutical and biomedical applications owing to their distinct physical chemical properties and multiple functionalization capabilities.CNTs are flexible and elasticand are very strong.These matenals have high electrical reaction.They have a significant chemical reaction.Nanotubes in nanotechnology are among the materials that are being considered in cancer and are being developed.Carbon nanotubes are nanometer_sized cylinders that consist exclusively of carbon atoms arranged in a hexagonal lattice.Diamonds are commonly known as stable and inert material.

Methods: CNTs with good penetrability,nano_needle shapes,hollow monolithic structures,optico_electrical properties,and high drug loading capacity have shown promising applicability for targeted cancer therapy,photo thermal ablation,and drug/gene delivery. Various treatment options have emerged in the past century for treating cancer.These include surgery,chemotherapy,radiation,immunotherapy,hormone therapy,genetherapy,photothermal therapy,photodynamic therapy,etc.However surgery,chemotherapy,radiation therapy,and their

combinations still remain the first lines of cancer treatment.Cancer is caused by unregulated proliferation of cells and chemotherapy targets to kill these cells.conventional chemotherapeutic agents fail to distinguish between cancer and normal cells and thus systemic administration of cancer chemotherapy leads to off_target adverse effects.

Results: The next step of carrying a drug to the target site is releasing the drug from the nanocarries.Smart nanocarries made from different stimuli_responsive materials can successfully do this.

Conclusion: Endogenous stimuli in crude low PH,hypoxia,redox reactions,and high enzymatic activity.Studies have demon strated the efficacy of CNTs in anticancer drug delivery

Keywords: Hypoxia ,CNT, gene therapy,flexible

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Cardiac Angiosarcoma: A Review of Clinical Symptoms, Diagnosis, Treatment, and Prognostic Factors (Review)

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Introduction: Cardiac tumors are a group of rare neoplasms that are associated with a high mortality rate. Most of these neoplasms are primary cardiac tumors (PCTs). Among them, patients with malignant primary cardiac tumors (MPCTs) usually have lower survival and higher mortality rates. Most malignant primary cardiac tumors are sarcomas, with one-, three-, and five-year survival rates of 46%, 22%, and 17%, respectively, reported in these patients. Angiosarcoma is one of the most common cardiac sarcomas, accounting for about half of all sarcomas. This malignancy is slightly more common in men and is usually diagnosed in patients aged 39 to 48.9 years with non-specific clinical symptoms. Despite the invasive nature of this malignancy and the high mortality rate in these patients, there is no specific guideline for timely diagnosis or appropriate treatment. Therefore, the aim of this study is to review the clinical symptoms, appropriate diagnostic modalities, effective treatment approaches, and determining the factors affecting the prognosis of these patients.

Methods: For this review study, a comprehensive search was conducted in PubMed, Web of Science, Scopus, and Google Scholar databases. After removing duplicate and non-English articles, cross-sectional, case-control, and case series articles were included in the study and review articles were excluded. Initially, to examine the thematic relationship of the articles, their titles and abstracts were evaluated, and after removing irrelevant articles, their full text was examined. The information from the articles was extracted and combined and compared with each other to obtain results.

Results: Cardiac angiosarcoma accounts for more than 50% of all cardiac sarcomas. The incidence of this malignancy is slightly higher in men and the average age of diagnosis is 44.4 years. It mainly presents with non-specific symptoms such as dyspnea, pericardial effusion, and chest pain, which is why most patients have been diagnosed with metastases to the lungs, liver, and bones at the time of diagnosis. The most common anatomical location of tumor is the right atrium, but it can also invade the pericardium, lymph nodes, and superior vena cava. The mortality rate of this malignancy is 64.7 to 100%, and most of these tumors are grade 3 or higher on pathological diagnosis.

According to studies, the most effective diagnostic modalities for the tumor are MRI, Transthoracic Echocardiography, or CT scan, and the most suitable modalities for diagnosing metastasis are CT scan, MRI, or PET/CT scan. The most effective treatment approach that has also been associated with increased patient survival, depending on the patient's condition, is Radical Resection with adjuvant chemotherapy. In some studies, radiotherapy has also been considered as a suitable approach to improve patient survival. The most important factors affecting the prognosis of the disease are age over 45 years, tumor size larger than 5 cm, local invasion and metastasis at the time of diagnosis, tumor histological grade, and the presence of tumor necrosis and cytogenetic aberrations such as 1q+.

Conclusion: Cardiac angiosarcoma is a rare malignancy that is associated with low survival rates and high mortality. This disease is accompanied by nonspecific clinical symptoms that can lead to delayed diagnosis and metastasis. Despite the invasive nature of this tumor, there is no suitable guideline for diagnosis, treatment, and prognosis of this disease. Knowledge of clinical symptoms, available diagnostic modalities, and appropriate treatment approaches can help physicians manage it. Finally, the development of multicenter clinical studies to identify effective diagnostic and therapeutic modalities, as well as laboratory studies to better understand the oncologic markers of this malignancy, seems essential.

Keywords: Primary Cardiac Tumor, Malignant Primary Cardiac Tumor, Angiosarcoma, Diagnosis

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CCNA2 and PLK1 as Prognostic Biomarkers in Prostate Cancer: The Cancer Genome Atlas Transcriptomic Analysis (Research Paper)

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Introduction: Prostate cancer (PCa) is the second most common cancer type in men after lung cancer [1, 2]. It is considered a major cause of death among men worldwide, posing a significant health burden. Despite advancements in diagnosis and treatment, the underlying molecular mechanisms of this disease remain unclear, making it challenging to manage. This study identified potential genes involved in PCa survival rates that could serve as biomarkers for its prognosis.

Methods: Firstly, RNA-seq data in raw format (STAR-Count) and clinical information of prostate adenocarcinoma (PRAD) was obtained from The Cancer Genome Atlas (TCGA) data portal through the “TCGAbiolinks” package and R programming language. Protein-coding genes were selected from the count expression matrix using the "biomaRt" package in R software. Furthermore, during the preprocessing procedure, genes with zero or near-zero expression were excluded based on CPM (Count per million<10 in 70% of samples) and the remaining expression matrix was normalized by “edgeR” package through TMM (trimmed mean of M-values) method. Using the “limma” package, data were converted into log2 scale and differentially expressed genes (DEGs) were identified from two distinct groups of normal and cancer according to the following criteria: $|log2FC| > 1$ and adj P-value < 0.01. The Database for Annotation, Visualization and Integrated Discovery (DAVID) was then used to elucidate potential GO function and signaling pathways (KEGG) related to DEGs. Moreover, univariate Cox regression analysis was employed to DEGs that are associated with survival outcomes (meeting the significance criterion of P<0.05). Following that, the protein-protein interaction (PPI) network was constructed by STRING and analyzed by Cytoscape software. Additionally, the degree of all nodes was calculated by the cytoHubba plugin with the focus on degree. Finally, the GEPIA2 database was utilized to draw Kaplan-Meier curves of hub genes.

Results: The count expression matrix consisted of 502 PCa patients and 52 normal samples with 60,660 genes. Eliminating genes with low expression values resulted in a reduced dataset containing 14,565 genes. After normalization, we had only 12,279 genes. In total, 1,899 DEGs (559 up-regulated genes and 1,340 down-regulated genes) were identified between PCa tissue samples and normal prostate samples. The GO analysis results were classified into molecular functions (MF), biological processes (BP) and cellular components (CC). For MF, DEGs were mainly associated with calcium ion binding (GO:0005509). In the CC category, DEGs were enriched in plasma membranes (GO:0005886), and as for BP, cell differentiation process (GO:0030154) was enriched. Furthermore, KEGG analysis indicated that DEGs were mainly enriched in neuroactive ligand-receptor interaction pathways. After performing univariate Cox regression analysis on DEGs, we found that the prognosis of 99 genes was statistically significant, which had $P<0.01$ and $HR>1$. Furthermore, we selected the top 10 degree through cytoHubba, of which only two were significantly associated with poor prognosis based on Kaplan-Meier curve and log-rank test ($P<0.05$): cyclin A2 (CCNA2) and polo-like kinase 1 (PLK1).

Conclusion: In the present study, a number of key genes and pathways were uncovered for prostate cancer. These genes may serve as biomarkers for poor prognosis and possible treatment targets.

Keywords: Prostate cancer, Biomarkers, Bioinformatics, Gene expression analysis, TCGA

CD8+ T cell dysfunction and Exhaustion in cancer (Review)

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Introduction: Introduction: CD8+ T cells certain for cancer cells are found in malignancy cells. Tumors do, however, continue to grow despite their presence. Immune checkpoint blockade and adoptive T cell therapy in clinical assessment was success and shows CD8+ T cells' potential to mediate reactions of antitumour; nevertheless, long-term responses to immunotherapy do not occur in most cancer patients. Cancer cells can be specifically found and eliminated by CD8+ T lymphocytes. Cancer patients have CD8+ T lymphocytes that are reactive against the antigens expressed by tumors, including self-antigens and tumor-specific neoantigens. Even tumors that express highly immunogenic neoantigens, however, frequently advance in spite of their existence. The presence of developing tumors with T cells shows that tumor-reactive CD8+ T cells degenerate throughout tumorigenesis. Tumour-infiltrating lymphocytes (TILs) reactive to tumor antigens express multiple inhibitory receptors (such as PD1 and CTLA4), also they have been a major source of information about CD8+ T cell dysfunction. While "dysfunctional" is the term we use to describe hyporesponsive T cells in cancer, other names like "anergy," "tolerance," and "exhaustion" are also frequently employed. We now go over how CD8+ T cells differentiate into dysfunctional states during the development of tumors. Tolerance In order to prevent autoimmunity, self-tolerance, or the hyporesponsive state of self-antigen-reactive T cells, is required. The main immunotherapy targets during the past few decades have been self-tumor antigens, including adoptive T cell therapies (such chimeric antigen receptor T cells). Despite the fact significant results have been shown in haematological cancers and melanoma, there are still limitations for targeting self-tumour antigens in other sorts of solid tumors. Neoantigen-specific T cells, in contrast to self-reactive T cells, are not constrained by central or peripheral self-tolerance mechanisms, and as a result, ought to demonstrate greater antitumor responses. Neoantigens, however, may be displayed in a non-inflammatory circumstances in the early stages of tumor formation, leading to a hyporesponsive T cell state analogous to the generation of peripheral self-tolerance. Ignorance T cells may be 'ignorant' of their cognate antigen and stay in a phenotypically antigen-inexperienced naive state in the case of self-antigens that are produced at low levels or in anatomical areas that are isolated from immunological recognition (immune privileged sites). If cancer cells overexpress these antigens during

development of tumor, it is possible to overcome this ignorance. In addition to the self-antigens, immunological ignorance can also affect tumor-specific neoantigens. For instance, early in the development of a tumor, transformed cells may be hidden within healthy tissues or organs and go undiscovered. As a result, T cells specific for tumor neoantigens could stay ignorant until tumors advance to the point when tumor antigens are presented in TDLNs (tumour-draining lymph nodes) and activate antigen-specific T cells. Anergy Anergy' means that T cells are less responsive when they are activated without inflammation and/or co-stimulatory signals. TCR engagement in the lack of co-stimulation does not effectively activate these pathways, resulting in anergy. 'Anergy' has been employed to explain T cell differentiation and dysfunction because naive tumour-specific T cells is primed suboptimally when they face an antigen on tumors or APCs that don’t express the co-stimulatory ligands (such as, CD80 or CD86). The hyporesponsive T cell states like Anergy and exhaustion are related to the dysfunctional differentiation of tumor-specific T cells exhaustion At the beginning, the term "exhaustion" was utilized to characterize the hyporesponsive T cell states that occur after chronic infections. Stimulation of chronic antigen causes "exhaustion," which is the progressive loss of effector functions. 'Exhaustion' has been utilized to explain T cell dysfunction in Created, advancing tumors because T cells in late-stage and progressing tumors become hyporesponsive as a result of repeated exposure to tumour antigens and share many essential characteristics with T cells in chronic infection

Methods: this is a review article and doesn't have this part

Results: this is a review article and doesn't have this part

Conclusion: Conclusion CD8+ T lymphocytes possess diverse modes of tumour eradication, including direct targeting of neoplastic cells and indirect targeting of tumour stromal cells. Current knowledge regarding the most pertinent mechanism(s) in human cancer, whether disparate tumours and T cells employ different mechanisms, and the subversion of these mechanisms in hyporesponsive tumour-infiltrating lymphocytes remains limited. The identification of tumour-reactive T cell subsets and their functional states in patients, coupled with comprehension of how these T cells execute antitumour effector function, will prove pivotal in comprehending and predicting the efficacy of immunotherapeutic strategies.

Keywords: Exhaustion, CD8+ T cell, cancer, Anergy

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Cell Therapy in Cancer Treatment (Review)

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Introduction: Cancer is an abnormal growth of cells whose proximate cause is an imbalance in cell proliferation and death that breaks the control and balance system normal physiological and whose ultimate cause is one or more of a variety of alterations genetics.

Methods: In this article, a collection of articles dealing with the topic of the proposed cell therapy in cancer treatment from pubmed, google scholar, nature databases with the keywords Cell therapy, Cancer management, Cancer treatment, Adoptive cell transfer, Cancer care, Cancer cells, CAR T-cell therapy,… were searched and finally 100 articles related to the subject were found and analyzed.

Results: The results of the studies showed: Clinical trials of cell therapy are currently continuing to many different types of cancer. Cell therapy is a type of treatment that involves using living cells to treat or prevent diseases. In cancer treatment, cell therapy is used to boost the immune system's ability to fight cancer cells or to directly target and destroy cancer cells. There are two main types of cell therapy used in cancer treatment: 1. Adoptive cell transfer (ACT): This involves taking immune cells from a patient's body, modifying them in the laboratory to enhance their ability to recognize and attack cancer cells, and then infusing them back into the patient's body. 2. CAR T-cell therapy: This involves genetically engineering a patient's T cells (a type of immune cell) to express chimeric antigen receptors that can recognize and bind to specific proteins on cancer cells. The modified T cells are then infused back into the patient's body to seek out and destroy cancer cells. Both ACT and CAR T-cell therapy have shown promising results in clinical trials for certain types of cancer, such as leukemia and lymphoma. More recently, scientists have developed new cancer therapies combining genetic and cellular therapies. Specifically, researchers have developed genes that encode artificial receptors that, when are expressed by immune cells, they allow these cells to recognize specifically cancer cells, thereby increasing the ability of these immune cells genetically modified to kill cancer cells in the patient. However, these therapies can also cause serious side effects, such as cytokine release syndrome and neurotoxicity, which require close monitoring and management.

Conclusion: In conclusion, cell therapy is an innovative approach to cancer treatment that has the potential to improve outcomes for patients with certain types of cancer. Researchers believe that this method may be promising in the future for patients with many types different from cancer. Cell therapy can be used as a novel and functional method for cancer treatment. Ongoing research is needed to further refine and optimize these therapies and to identify which patients are most likely to benefit from them.

Keywords: Cell therapy; Cancer treatment; Adoptive cell transfer; cancer cells

cervical cancer (Review)

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Introduction: Cervical cancer is the fourth common gynecological malignancy disorders and second leading cause of cancer associated female mortality in many less developed countries. The disease is most commonly diagnosed in the fifth decade of life several years earlier than medien age at diagnosis of breast , lung and ovarian cancers . the main causes are repeated contact with high risk hpv virus(which is transmitted through sex), weak immune system and smoking .many of high risk hpv types can cause anogenital cancers . between high risk hpv types that cause anogenital cancer ,types 16,18,31,35,39,45,51,52,56,58 cause most invasive cancers.cerviacal cancer is characterized by symptoms of bleeding after intercourses, abnormal bleeding between periods , chronic pelvic pains, and a feeling of pelvic pressure .According to figo classification cervical cancer is classified into following groups :stage 0:carcinum in sito , stage 1:invasive carcinoma strictly confined to cervix, stage 2:carcinoma extending beyond cervix but not to pelvic sidewall, stage 3: carcinoma extending anto pelvicwall, stage4:carcinoma extends beyond the true pelvic wall or clinically involves mucosa of bladder or rectum. Treatment according to the stage of diagnosis includes hysterectomy, chemotherapy, radiotherapy or a combination of these.

Methods: the present literature review was performed using pubmed (national institute of health .ncbi.nlm.nih.gov/pubmed) , scopus (elsevier, scopus.com/scopus/home.url)and web of knowledge(thomson reuters,wok.mimas.ac.uk)electronic databases,and the following key words were searched:cervical cancer, epigenetic changes in cervical cancer . several article were found in the surveyed databases and only the most relevant ones published in high impact factor journals and conducted by groups with recognized knowledge in the area were selected .

Results: cervical cancer can develop in about 500000 women in year. Recent studies have shown the correlation between epigenetics and development and progression of cervical cancer. Among the epigenetic modifications, the role of candidate gene DNA methylation in cervical cancer has been studied the most. Accumulated DNA methylation in specific genes is detected as early signatures of malignant cervical cancer . High-risk HPV viruses , especially

types 16 and 18, are responsible for these cell changes or dysplasia , especially in 80% squamous cells and less in 20% cylindrical cells of the cervix. . Cervical cell dysplasia is divided into three degrees before cervical cancer. Dysplasia type 1 or cin 1, which is called mild dysplasia, is improved in most cases with expectant treatment or freezing. Dysplasia type 2 or CIN 2, which has involved two thirds of the cervix, treatment includes colposcopy or biopsy of the changed tissue seen in colposcopy in terms of transformation and visualization of cancerous cells or loop or conization or cone removal or cold knife to remove the changed tissue In case of no improvement . expectant treatment like , pap smear and vaginal exam should be repeated every six months for two years, and in case of no improvement or progress to the third stage or CIN 3, where three quarters of the cervix is involved, the treatment includes removal of the lesion or hysterectomy in the operating room at an advanced age.

Conclusion: Cervical cancer, although after breast and ovarian cancer, threatens the health of women of reproductive age, but by performing a series of diagnostic tests such as a pap smear from the age of twenty, if sexual activity begins,once a year for three years, and if the pap smear is normal,repeated every three years. and from the age of 30, performing HPV typing along with Pap smear every five years, as well as avoiding high-risk behaviors such as multiple sexual partners, not using condoms, and smoking can be diagnosed, prevented, and treated.

Keywords: cervical cancer, epigenetic, methylation, cin, pap amear

Characteristics and outcomes of patients with hepatitis-associated aplastic anemia: Treatment approaches in the last decade (Review)

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Introduction: Hepatitis-associated aplastic anemia (HAAA) is a rare but well-recognized subtype of acquired aplastic anemia characterized by pancytopenia 1–3 months following an episode of acute hepatitis. In this syndrome, bone marrow failure results in a decrease in RBCs, WBCs, and platelets, followed by hepatitis as a result of decreased production. Other than drugs, toxins, and viral infections, aplastic anemia arises from an abnormal immune response. Acute hepatitis B-associated aplastic anemia is an extremely rare form of aplastic anemia. Typically, hepatitis is either idiopathic or caused by one or more hepatitis viruses, parvovirus B19, cytomegaloviruses, Epstein-Barr viruses, or toxins. The symptoms can range from fatigue to shortness of breath to increased susceptibility to infections caused by pancytopenia. Patients may also present with pallor, petechial rashes, ecchymosis, or signs of systemic infection on examination. The diagnosis is based on a prior history of hepatitis and pancytopenia in the complete blood count. A bone marrow biopsy typically indicates profound hypocellularity with morphologically normal residual hematopoietic cells in the absence of malignant infiltration and fibrosis. Since HAAA has a very poor prognosis, early detection is essential. For treating this syndrome, a variety of treatment options have been developed over the past decade based on each patient's condition.

Methods: The present study used scientific search by searching keywords and gathering related articles in databases including Science Direct, Google Scholar, and PubMed.

Results: There are a number of treatments for aplastic anemia that aim to achieve hematopoietic recovery, including immunosuppressive therapy (IST), thrombopoietin receptor agonists (TPO-RA), allogeneic stem cell transplantation (allo-HSCT), and anabolic hormones. Combining TPO-RA with immunotherapy along with cyclosporine and anti-thymocyte globulin is the

most effective drug therapy. As a primary treatment option when a sibling with identical human leukocyte antigen (HLA) is available, allogeneic HSCT is often preferred. In the absence of a suitable donor, IST is an option that involves combining bone marrow stem cells from a sibling or cord blood stem cells from an unrelated donor. IST involves the use of immunosuppressive drugs, such as horse or rabbit antithymocyte globulins (ATG), antilymphocyte globulins (ALG), cyclosporine A (CsA), corticosteroids, and sometimes granulocyte colony-stimulating factor (G-CSF). An earlier study found that rATG was superior to horse ATG (hATG) in terms of effectiveness. As well as IST being effective post-transplantation, romiplostim, a thrombopoietin receptor agonist, and IST have been used effectively in the case of a child with severe HAAA who underwent liver transplantation. As well as platelet transfusions, coagulation factor replacement, and iron chelation therapy, supportive care measures are crucial in the early stages of this condition. A broad-spectrum antibiotic and antifungal should be considered first in pancytopenia. New treatments are being explored, including rituximab, which can be used in refractory cases, and thrombopoietin receptor agonists, such as eltrombopag, which can be used in conjunction with immunosuppressive therapy to improve outcomes. For hepatitis B-associated HAAA, lamivudine or tenofovir can be used, and for Epstein-Barr virus-induced aplastic anemia, acyclovir can be used. In EBV-associated HAAA, eltrombopag, an oral thrombopoietin receptor agonist, was prescribed along with an immunosuppressive regimen consisting of rATG and cyclosporine. The use of umbilical cord blood transplantation as well as haploidentical transplantation may be considered if the patient does not respond to IST. Aplastic anemia has been investigated for the potential of mesenchymal stromal cells (MSCs) derived from several sources, including the umbilical cord (UC). As UC-derived MSCs are considered safe and genetically stable, they are ideal for therapy applications. In pediatric patients with severe aplastic anemia, UC-MSCs can be effectively used as part of a treatment with drugs like CsA.

Conclusion: To conclude, HAAA treatments encompass a range of choices, with the choice dependent on factors such as donor availability and the subtype of the disease. There is a low transplant-related mortality rate with allogeneic HSCT for hepatitis-associated aplastic anemia. It is likely that emerging therapies will lead to improved outcomes for individuals with this challenging condition, including MSC-based treatments and CsA combinations. Further, results suggest that IST combined with TPO receptor agonists may provide an effective treatment option for patients suffering from HAA who are undergoing LDLT.

Keywords: hepatitis-associated aplastic anemia, hepatitis, immunosuppressive therapy, allogeneic hematopoietic

Characterization and Evaluation of Nanofiber Materials at wound dressings (Review)

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Introduction: Nanofiber materials have high surface area-to-volume ratios, and their properties differ significantly from those of bulk materials. Therefore, their characterization and evaluation require different techniques than materials. Nanofiber materials can be characterized by various such as scanning electron microscopy, transmission electron microscopy, Fourier transform infrared spectroscopy, X-ray diffraction, and Thermogravimetric analysis. These techniques describe key structural and physicochemical properties such as size, morphology, surface area, porosity, and specific surface area The evaluation of nanofiber materials is mainly based on their performance concerning special applications such as filtration, catalysis, sensors, and wound. Materials selection, synthesis, analyses, and characterization are essential for successful nanofiber materials. Understanding the characterization and evaluation techniques for nanofiber materials is critical for their efficient use in applications.

Methods: Nanofiber materials are produced by various methods, including electroinning, template synthesis, self-assembly, and phase separation. These have a broad range of applications in various fields, including biomedical, energy storage, filtration, and sensors. In recent years, there has been an increasing interest in the characterization and evaluation of nanofiber materials understand their fundamental properties and optimize their performance for specific applications. Different characterization techniques, such as SEM, TEM, AFM, XRD, and FTIR, are used to examine the nanofiber morphology, properties, and structure. The evaluation of nanofiber materials involves testing their mechanical, electrical, thermal, and optical properties, as well as their biocompatibility toxicity.

Results: The fabricated nanofiber wound dressings, with their enhanced properties and characteristics, are expected to have a significant impact on wound healing. Due to their more orderly arrangement and improved structural integrity, the nanofiber wound dressings demonstrate enhanced mechanical strength, moisture retention capability, gas exchange capability,

and exudate absorption capacity compared to traditional wound dressings. These properties contribute to creating a favorable environment for wound healing by providing adequate support, moisture regulation, and oxygen exchange, which are crucial for the proliferation and migration of cells involved in the wound-healing process.

Conclusion: In conclusion, nanofiber wound dressings have shown promising results in terms of their impact on wound healing and have been extensively explored for their application in medicine. However, there are still challenges to overcome, such as the need for further clinical trials and validation of their effectiveness, addressing the cost-effectiveness of large-scale production, optimizing fabrication techniques, and exploring functionalization methods and integration of nanoparticles or nanocomposites. Further research should be conducted to address these limitations and advancements in the field of nanofiber wound dressings have the potential to revolutionize the way we treat and heal wounds. As a result, this could lead to improved patient outcomes and reduced healthcare costs in the future. Further research and development efforts are needed to optimize the fabrication techniques of nanofiber wound dressings in order to enhance their mechanical strength and structural integrity. Furthermore, functionalization methods should be explored to enhance the properties of nanofiber wound dressings, such as incorporating growth factors or bioactive molecules for enhanced tissue regeneration. Additionally, the integration of nanoparticles or nanocomposites into nanofiber wound dressings should be further investigated to enhance their therapeutic capabilities, including antibacterial.

Keywords: characterization, nanofiber, wound dressings

Characterization and investigation of cytotoxicity and antimicrobial properties of coencapsulated limonene and thymol into the Ferula assafoetida gum microparticles (Research Paper)

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Introduction: The connection between antimicrobial resistance and a heightened risk of treatment failure and recurrence is well-established. The six hospital-acquired pathogens, namely Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp., are collectively referred to by the acronym ESKAPE are the main culprits behind hospital infections worldwide, with a majority being multidrug-resistant strains, thereby posing a significant challenge to clinical practice. Thymol (Th) is derived from cymene and is a naturally occurring phenol monoterpene. It is an isomer of carvacrol. D-limonene (L) is a vital element of citrus flavor obtained from the peel and pulp of citrus fruits. Both limonene and thymol exhibit low stability and are prone to oxidation when exposed to air, light, humidity, and high temperatures. In this study, encapsulation of Th and L in Assafoetida gum (AFG) was investigated.

Methods: The characterization of the obtained encapsulated complexes was done by scanning electron microscope (SEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and thermogravimetric analyzer (TGA). Also, Encapsulation efficiency, and antibacterial properties of the free L and Th and encapsulated ones measured. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) L, Th, AFG, L-AFG, Th-AFG, and L-Th-AFG was evaluated. The checkerboard technique was used to evaluate the synergistic effects of the selected complex, imipenem and vancomycin were used against gram-negative and gram-positive drug-resistant bacteria of ESKAPE pathogens, respectively. MTT colourimetric assays of L, Th, L-AFG, Th-AFG, and L-Th-AFG were performed against fibroblast L929, Hella, and CT26 cell lines. The apoptosis evaluation was carried out according to the manufacturer's instructions using a FITC Annexin V Apoptosis Detection Kit with PI from BioLegend® (San Diego, California).

Results: The results of FTIR and XRD confirmed the incorporation of Th and L into the AFG. Thermogravimetric analysis indicated that the inclusion complex of AFG-Th enhanced the thermal stability of Th significantly. The inclusion complex of Th into the AFG increased its antibacterial activity. Minimum inhibitory concentration of Th was decreased after encapsulation into the AFG. FIC values for Pseudomonas aeruginosa showed additive effects and FIC of other bacteria showed synergism effect. The lowest cytotoxicity was for encapsulated L-AFG against Hella cell line with IC50 of 2755 µg/ml. There was a significance difference between the IC50 of encapsulated Th-AFG against fibroblast L929 and Hella cell line.

Conclusion: The results suggest that AFG-Th can potentially be used as a delivery system for hydrophobic and sensitive compounds to increase their usage in the pharmaceutical and food industries.

Keywords: Thymol, D-Limonene, Assafoetida gum , Encapsulation

Characterization and structure determination of a potent potassium channel blocker neurotoxin from the venom gland of Mesoburhus eupeus (Research Paper)

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Introduction: Scorpion venom is a great source of potent pharmacologically active agents. Different studies demonstrate the pharmacological effect of venom components for treatment of various diseases, including cancer, microbial, autoimmune and cardiovascular diseases. Moreover, some crucial enzymes such as phospholipase (A, B, C, and D), hyaluronidase, enolase along with toxins affecting ion channels (Na+, K+, Ca2+, Cl-) make an important part of the scorpion venom. Mesobuthus eupeus, a member of Buthidae family, is the most frequent scorpion species living in Iran. It is responsible for many of reported scorpion stings referring to hospitals and health centres. Prescience of some short chain and low molecular weight neurotoxins have been demonstrated in the venom of this scorpion.

Methods: In the present study, we analysed the transcriptome of the venom gland of M. eupeus obtained using total RNA extraction and cDNA library synthesis. The final transcriptome was blasted against peptides and proteins databases, including Uniprot and NCBI, in order to find a potassium channel blocker neurotoxin. Bioinformatics software was applied to analysis the physico-chemical properties of the identified protein. Three-dimensional structure of the protein was achieved by homology modelling. MD simulation was finally run to assess the protein structure.

Results: A potent potassium channel blocker was found in the transcriptome of the venom gland of M. eupes. It was submitted to the Gen Bank under the name of meuK-toxin. It is a water-soluble peptide with molecular weight of, 4271 g/mol and theoretical pI of 4.47. The structure of meuK-toxin consists of a conserved LCN-type cysteine-stabilized alpha/beta domain. This domain is stabilized by six cysteine residues. meuK-toxin is structurally analogous to scorpion toxins specific for apamin-sensitive potassium channel.

Conclusion: Here we found and characterized a small, potent potassium channel blocker derived from a scorpion venom gland. This gives us a basis information keys to investigate the function of this protein in future to define

underlying physiological processes or maybe design new selective useful drug.

Keywords: Potassium channel blockers, Mesobuthus eupeus, Transcriptome, Venom gland components

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Characterization of Disinfectant Susceptibility Patterns in Serratia marcescens isolates Collected from Hospitals in Ardabil province, Iran (Research Paper)

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Introduction: Antimicrobial biocides are extensively used for a long period to control hospital-acquired infections worldwide. Prolonged exposure of bacteria could promote development of resistance to antimicrobial biocides. The aim of this study was to evaluate the antimicrobial activity of four commonly used biocides i.e. triclosan, chlorhexidine digluconate, benzalkonium chloride and formaldehyde against Serratia marcescens isolates and to determine the prevalence of biocide tolerance related genes including qacE, qacED1, emrA, aceI, and fabI.

Methods: A total of 100 clinical isolates of Serratia marcescens were included in current study. The minimum inhibitroy concentrations (MICs) of antimicrobial biocides were measured using agar dilution method. Genes involved in the resistance to biocides were investigated by PCR method.

Results: The benzalkonium chloride MICs ranged between 32 -128 µg/mL, chlorhexidine digluconate 8 - 64 µg/mL, triclosan 1-32 µg/mL and formaldehyde 128 µg/mL. Overall, the highest MIC90 value was identified for formaldehyde (128 µg/mL) followed by benzalkonium chloride and chlorhexidine digluconate (64 µg/mL for each one) and triclosan 4 µg/mL. In present study, the qacE, qacED1, emrA, aceI and fabI genes were found in 91%, 55%, 100%, 88% and 82% of isolates, respectively. The qacG gene was not identified in our Serratia marcescens isolates. A significant association ($P < 0.05$) was observed between MICs of benzalkonium chloride and chlorhexidin with qacE and aceI genes. The presence of fabI gene was conversely associated with triclosan elevated MICs.

Conclusion: The results of this study indicated that triclosan was the most effective biocide against Serratia marcescens.

Keywords: Serratia marcescens, Disinfectant, Ventilators, qac genes

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Characterization of RBK cell line as a sensitive cell to bovine Herpesvirus-1 (BoHV-1) (Research Paper)

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Introduction: Viruses are obligate parasites and are completely dependent on host cells for survival and replication. RBK cell line developed and introduced by Razi Vaccine and Serum Research Institute, has been successfully established as a continuous cell line over successive passages.

Methods: RBK cells demonstrate marked sensitivity to certain viruses. In this experimental study, RBK cell line has shown significant sensitivity to BoHV-1 virus. At present research, the characteristics of RBK cell line were performed by molecular and karyotype methods, as well as growth characteristics. Cloning of the RBK cell line was performed using limited dilution method in parallel with analytics for characterization of each cell clone quantitatively and qualitatively. Then four cell clones were compared based on their sensitivity to the BoHV-1 virus.

Results: in this study, the RBK-D5 clone was selected as the most appropriate cell line for further study and was subjected to tests for identity, chromosomal analysis and doubling time. In the end, RBKD5 in terms of species origin and contamination-free was confirmed by PCR method, as well as RFLP-PCR and Real-time PCR. We observed that the cell line directed towards karyotype diversity, because of aneuploidy. Aneuploidy itself can be responsible for the procreation of chromosomal instability. Karyotype diversity represent chromosomal changes in the continuous cell line that carries the characteristic of immortalized cell line.

Conclusion: In general, one of the key factors in virus isolation is multiplication speed in cell culture and high production efficiency. Therefore, it's absolutely necessary to choosing a suitable cell line with high sensitivity to certain virus. At present study, our results revealed that RBK-D5 cell line contain high growth rate, stability and surprisingly sensitive to BOHV-1 virus at different passages, as well as our results confirmed the absence of contamination to other cells and unwanted factors. In total, the conducted investigations confirm the capability of the studied cell. As a conclusion the RBK cell line can be widely used in research, detection, virus propagation and virus quality control or titration.

Keywords: RBK cell line, BoHV-1 virus, karyotype

CHAuNP affect the human colorectal adenocarcinoma cell line's clonogenicity and mitochondrial membrane potential (Δψm) (Research Paper)

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Introduction: In the world, CRC is the third most common cancer that kills people of both sexes. Nanoparticles have been introduced as a promising and potentially effective approach for the treatment of tumors as a result of the use of nanotechnology in medicine. Gold nanoparticles have special physicochemical characteristics that allow them to influence critical cancer cell activities.

Methods: We employed the human colorectal adenocarcinoma cell line HT-29 for this study. covering chitosan Gold nanoparticles were synthesized chemically. The size distribution, surface plasmon resonance, and imaging were analyzed using DLS, visible-ultraviolet (UV-VIS) spectroscopy, and atomic force microscopy, respectively. Cell survival and metabolic activity were assessed using the MTT test, and the IC-50 of gold nanoparticles was determined. Flow cytometry Annexin V-FITC / PI was used to evaluate apoptosis. The mitochondrial membrane potential (Δψm)was measured using Rhoudamin123. Reactive oxygen species were measured using the DCFH-DA method (ROS). Colony formation capacity was evaluated using a clonogenic assay method. The relative expression of Gene expression was quantified using the real-time qRCR technique.

Results: The chitosan-coated gold nanoparticles were spherical in shape, with an average size of 12.3 nm and a surface plasmon resonance at 520 nm. 33 μM was the evaluated IC-50 for gold nanoparticles. In comparison to the control group, the nanoparticles markedly limit colony formation, diminish mitochondrial membrane potential, and trigger apoptosis in HT-29 cells. Additionally, there was no significant alteration in the level of reactive oxygen species produced. Genes involved in apoptosis and anti-apoptosis

respectively showed a significant increase and decrease in their relative expression.

Conclusion: The evidence suggests that gold nanoparticles coated with chitosan have a cytotoxic effect on human colorectal adenocarcinoma, indicating that they can be further investigated as a therapeutic agent.

Keywords: Gold nanoparticles, chitosan, colorectal cancer, apoptosis, mitochondrial membrane potential, reacti

Chimeric Antigen Receptor (CAR) NK Cell Therapy in Multiple Myeloma (Review)

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Introduction: Multiple myeloma (MM) is an incurable disease with a collection of enfeeblement hematological disorders with ordinary clinical phenotype that occurs by atypical plasma cells originate from terminally differentiated lymphoid B-cell lineage. Multiple myeloma is the second most common hematological cancer after Non-Hodgkin lymphoma (NHL) and accounts for approximately 1% of all malignancies. Natural Killer (NK) cells are part of natural armament were described as large granular lymphocyte, manifesting 5-20% of circulating lymphocytes in humans which are capable to annihilate unnatural cells without the request for prior confronting. With the remarkable capability of NK cells to efficiently induce cytotoxicity without prior antigenic stimulation, antigen presentation by MHC class I molecules, and antibody recognition, it is achieved through a complex interplay between inhibitory such as Killer immunoglobulin-like receptor (KIRs) and activating receptors like Natural cytotoxicity receptor (NCR) family. These receptors and their signals involve the release of cytokines, induction of apoptosis, and ultimately the elimination of cancer cells. Genetic engineering enables the use of synthetic receptors to alter the specificity and function of NK cells. Unlike T-cells, NK cells are considered to be safer effector cells, as they have the potential to avoid serious complications such as cytokine release syndrome (CRS), tumor lysis syndrome, graft versus host disease (GVHD), and neurotoxicity.

Methods: A search was conducted in PubMed and Google Scholar using the keywords “Multiple myeloma”, “CAR-NK Cells” and “Natural Killer cells”. The relevant documents were selected, and a thorough review of the information was completed. There are various sources for CAR-expressing NK cells to produce large-scale off-the-shelf products. These including peripheral blood mononuclear cells (PBMCs), which typically have a mature phenotype and are easily isolated. Umbilical cord blood (UCB) is advantageous for selecting donors with certain HLA types and less mature phenotype. NK92 cell lines are less cytotoxic and more affordable. Human-induced pluripotent stem cells (iPSCs) demonstrate a mature phenotype and antitumor cytotoxicity. CAR constructs are typically made up of an extracellular synthetic receptor that recognizes antigens, an extracellular hinge region, a transmembrane domain,

and one or more intracellular co-stimulatory domains. The CAR receptor is usually derived from a murine monoclonal Antibody in the form of a single-chain variable fragment (scFv), although it can also be encoded to express a naturally occurring surface receptor that has an affinity for tumor-specific ligands. Various methods of gene transfer have been utilized in NK cells, including Non-viral delivery methods (e.g. Electroporation and Cell squeezing), Viral-vectors (Retroviral and Lentiviral vectors), gene-editing techniques (like CRISPR/CAS 9 and Transposons), and Surface engineering approaches (e.g. Liposomes).

Results: Chimeric antigen receptor NK (CAR-NK) cells have shown promise as a type of Adoptive NK cell therapy against MM. These cells have the ability to kill myeloma cells, while also being mostly non-toxic to normal tissues. Thanks to Advancements in gene-editing techniques, new CAR-NK cell products with potent anti-tumor activity have been developed. This can greatly improve the survival rates of cancer patients who have limited treatment options. As the enthusiasm for innovative immunomodulatory therapies grows, there is a chance for even greater effectiveness in targeting NK cells against myeloma. With more clinical data expected in the coming years, CAR-NK cell therapies could potentially revolutionize tumor immunotherapy. As a result, the use of allogeneic NK cells as immunotherapy for MM holds great promise

Conclusion: This review describes the principle design of CARs, the main genetic modification techniques, and the potential uses in the treatment of multiple myeloma. The use of Chimeric Antigen Receptor NK cells for adoptive cellular therapy shows promise and possesses the potential to be developed as readily available “off-the-shelf” products, it offers an interesting strategy to treat MM patients in clinical use.

Keywords: Multiple myeloma_ CAR-NK Therapy_ Natural Killer cells

Chimeric Antigen Receptor (CAR) NK Cell Therapy VS CAR-T Therapy in Multiple Myeloma. (Review)

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Introduction: Multiple myeloma (MM) is a heterogeneous, incurable plasma cell malignancy associated with an overproduction of monoclonal gammaglobulin (also known as M protein). This condition represents approximately 10-15% of all hematological malignancies. MM is also known as Kahler's disease, most commonly presence of hypercalcemia, renal insufficiency, anemia and lytic bone lesions (CRAB features) with a median age of diagnosis 65-72 years. Chimeric antigen receptor (CAR) T cell therapy is a remarkably personalized immunotherapy that utilizes genetically modified T cells, primarily CD8+ cytotoxic T lymphocytes (CTLs), along with monoclonal antibodies (mAb). This innovative approach aims to effectively target and eradicate tumor cells independently of human leukocyte antigen (HLA) presentation. Natural killer (NK) cells used in CAR-NK therapy are crucial components of the innate immune system, possessing cytotoxic abilities similar to CTLs. Additionally, this cells possess synthetic receptors, enabling them to eliminate target cells without the need for prior antigen confrontation.

Methods: A search was conducted in Google Scholar and PubMed using the keywords "multiple myeloma", "CAR-T Cells", "CAR-NK Cells", and "Natural Killer cells". The relevant documents were carefully adopted, and a comprehensive review of the information was carried out. CAR constructs in NK cells, which bear similarity to T cells, consist of an extracellular synthetic receptor (Ectodomain) derived from a mAb for recognizing tumor-associated antigens (TAAs). They also include an extracellular hinge region (spacer), a transmembrane domain (a hydrophobic region), and at least one intracellular signaling domain (endodomain), which serves as the functional terminus of the CAR. The activation signaling pathways through the endodomain enhances the elimination of tumor cells. In CAR-T cell therapy, the synthesis of CARs is autologous, involving the collection of the patient's own peripheral blood mononuclear cells (PBMCs). In CAR-NK therapy, NK cells can be derived from various sources, such as NK-92 cell lines, human-induced pluripotent stem cells (iPSCs), or healthy donors (allogeneic). CAR-NK cells and CAR-T cells are produced ex vivo through a series of steps including stimulation of T/NK cells, genetically engineering using various system (such

as viral vectors, transposon, and CRISPR/CAS 9), proliferation, and finally, the infusion of CAR cells into the body.

Results: The significant advantage of CAR-T cells is their long-term working ability. Compared to other myeloma treatments, a single infusion of CAR-T cells may lead to persistent immunity and strong cytotoxicity. The disadvantages of this therapy are long-term production time, graft versus host disease (GVHD), cytokine release syndrome (CRS), and neurotoxicity. Other side effects of CAR-T therapy include B-cell aplasia and grade III/IV anemias that considered of on-target/off-tumor toxicity (OTOT). In contrast to CAR-T cells, CAR-NK cells are safer effector cells that may abstain or decline adverse effects of multiple myeloma such as tumor lysis syndrome, CRS, GVHD, and other OTOTs of CAR-T therapy. Furthermore, it is cost-beneficial therapy due to the attempt to make off-the-shelf products. Disadvantages of CAR-NK therapy are lack of clonal expansion that would limit clinical utility and obstacles in freezing and storage.

Conclusion: This review provides an overview of the main design of CARs, compares of CAR-T and CAR-NK therapy, discussing their potential application in the treatment of multiple myeloma. The positive results achieved with CAR-T/NK cell therapies have strengthened the field of myeloma immunotherapy. However, it is important to address the limitations of these technologies through additional research on CARs and finding solutions for the obstacles based by CAR-NK/T cells. By doing so, the treatment of multiple myeloma will become more accessible.

Keywords: Multiple myeloma_ CAR-NK cell Therapy_ CAR-T cell therapy_ Natural Killer cells

Clinical Implications of Subclinical Hypothyroidism on Sperm Quality: A Systematic Review and Meta-Analysis (Review)

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Introduction: Background: Cytokines such as tumor necrosis factor alpha play roles in the tumor microenvironment by affecting aspects of cancer progression. The goal of this study was to investigate how these cytokines impact tumor cell growth and spread through methods and a systematic review.

Methods: Methods: We conducted experiments using both laboratory and animal models to assess how TNF α influence tumor cell proliferation, invasion and metastasis. Additionally we performed a review by analyzing existing literature to gather evidence on the role of these cytokines in cancer progression.

Results: Results: Our findings from the experiments showed that TNF α have effects on different types of cancers. While some cytokines promote cell growth others exhibit effects. Moreover these cytokines demonstrate nuanced roles in tumor metastasis by influencing migration and invasion capabilities. The systematic review supported these multifaceted roles by highlighting context influences on tumor progression across malignancies.

Conclusion: Conclusion: This comprehensive study provides insights into the relationship between TNF α in terms of tumor cell growth and metastasis. It emphasizes that their effects are specific, to the context in which they occur. These findings highlight the possibility of using modulation as a basis, for

therapeutic approaches, which opens up exciting prospects for further research and the development of cancer treatments, in the future.

Keywords: Keywords: Neoplasm, Tumor necrosis alpha, Metastasis, Proliferation, Systematic Review

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Clinical methods of Alzheimer's treatment: A Systematic review (Review)

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Introduction: Alzheimer's disease is a neurodegenerative disease caused by amyloid beta protein. According to the statistics of the World Health Organization, it is predicted that the prevalence of Alzheimer's disease will increase four times by 2050, while today it is the fifth cause of death among people over 65 years old. This disease imposed a lot of treatment costs on countries, and no cure was found for this disease

Methods: We systematically reviewed Alzheimer's clinical studies with the aim of identifying a better and effective way to treat Alzheimer's disease. For this purpose, English language clinical trial articles between 2017 and 2023 were searched in PubMed, Cochrane and Science Direct databases. The titles of the articles were scanned with keywords "Alzheimer's" and "treatment".

Results: After studying the abstract, conclusion, results and discussion sections of the selected articles, into five categories: 1) Radiation and electromagnetic therapy, which in this method enhances cognitive function. 2) Biomarkers, in this method, with the help of these biomarkers, drugs are provided that identify destructive proteins in the brain and can slow down or eliminate Alzheimer's disease. 3) Antibody, for example Donanemab, which targets the amyloid beta protein in the brain and destroys it. 4) A hormone, for example, the incretin hormone GLP-1, which causes the recovery of glucose in the blood-brain barrier, which in turn leads to the protection of Alzheimer's against cognitive disorders. 5) A drug that was seen to have effects on behavioral performance and Alzheimer's improvement in this method; Was divided. Among the 28 articles that entered the study phase, 4 articles are in the first category, 2 articles in the second category, 1 article in the third category, 2 articles in the fourth category and 19 articles in the fifth category. In this research, 14.2% of treatment methods are related to the first category, 7.1% are related to the second category, 3.5% are related to the third category, 7.1% are related to the fourth category and 67.8% are related to the fifth category.

Conclusion: It seems that according to the above research methods, there is a prospect of improving the treatment of Alzheimer's disease, but each of them has challenges such as lack of time and small sample size. In general, the clinical trials conducted on Alzheimer's disease were mostly medicinal.

Keywords: Alzheimer's disease, Clinical trial, treatment

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Cloning and expression of Clostridium novyi phospholypase C toxin in prokaryotic host (Research Paper)

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Introduction: Cancer is one of the genetic diseases, breast cancer is one of the commonest of them and the first cause of death in women. Bacteria are used in different ways in cancer treatment such as: gene transfer system by vector, bacterial toxin and spore. Clostridium novyi, a gram-positive bacillus, is an obligate anaerobes with spore. This bacterium by producing phospholipase C enzyme and interacting with the membrane of eukaryotic cells causes cell lysis. Due to the cytotoxic characteristic and role of the enzyme in the pathogenesis of the disease, It can establish one of the main components of immunotoxin or vaccine. The aim of the present study is cloning the PLC-Darpin gene in the pET28a vector and express the protein in the bacteria of Escherichia coli.

Methods: The sequence of PLC-Darpin gene was amplified by using specific primers with PCR method, PCR products and pET28a plasmid were cut with restriction enzymes NdeI and XhoI and the considered segment was conjuncted to the cut vector and then transformed into Ecoli BL21(DE3) and screened by the antibiotic of canamaycin. Colonies were evaluated by PCR method and positive colony plasmid was screened by double digestion method and Protein expression was analyzed by using SDS-PAGE gel, Finally it was checked with specific antibody by using western blotting method.

Results: The size of the amplified fragment which is about 1600 bp was confirmed by PCR and using agarose gel. The cut plasmid pET28a after inserted fragment confirmed the enzymatic activity. The cloned fragment was confirmed by using the PCR colony method and the addition of IPTG caused the expression of PLC-Darpin protein, which size was about 60 kDa, about 3

hours after induction, eventually protein expression by using western blotting method was confirmed.

Conclusion: Due to the enzymatic role and characteristic cytotoxic of phospholipase C in Clostridium novi, it can create one of the main components of immunotoxin or vaccine.

Keywords: E. coli BL21(DE3), Cloning, Clostridium Novyi, SDS-PAGE, Western blotting

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Clostridium bacteria: The team of microscopic oncologists (Review)

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Introduction: As we approach the year 2023, the global rise in cancer mortality remains a pressing concern. Recent studies have demonstrated the remarkable potential of bacteria in combating cancer by stimulating the immune system. Exciting evidence suggests that bacterial therapy can revolutionize both the treatment and diagnosis of tumors. To effectively classify and treat tumors, the introduction of obligate or optional anaerobic bacteria into solid tumors may be necessary. Notably, certain strains of Clostridium have proven to be particularly effective in cancer treatment. A fascinating natural phenomenon lies in the ability of Clostridium spores to infiltrate tumors and selectively germinate in hypoxic regions within dense tumors upon injection into a vein. This bacterial invasion directly eliminates tumor cells by enhancing the presence of tumor-specific antigens, enabling the immune system to recognize and attack cancerous cells. Although these bacteria do not directly destroy tumor cells, their activation of the immune system holds great promise for eradicating them.

Methods: Currently, an extensive range of bacteria is employed for cancer treatment, designing bacteria-carrying pharmaceutical compounds, and facilitating radiotherapy or radiation therapy. Additionally, genetic manipulation techniques can enable bacteria to specifically target tumor tissue and inhibit angiogenesis.

Results: In this comprehensive review, we delve into the potential advantages of utilizing Clostridium bacteria in cancer medications. Specifically, we explore the abilities of Clostridium perfringens and Clostridium novi to induce angiogenesis, provoke immune responses, and operate within oxygen-deprived environments.

Conclusion: In conclusion, Clostridium bacteria hold great promise in the field of cancer treatment. Their immunomodulatory effects, anti-inflammatory properties, and potential to enhance drug efficacy make them an exciting area of research. As we continue to unravel the intricate Harnessing the power of clostridium bacteria relationship between bacteria and cancer, it is clear that Closterium bacteria have the potential to revolutionize cancer treatment and improve patient outcomes. Further research and clinical trials are needed to fully understand the mechanisms and therapeutic applications of these remarkable bacteria. As the research continues, the potential of Clostridium bacteria as a natural and effective treatment for cancer is becoming increasingly clear. The implications of this research are immense and could revolutionize cancer treatment as we know it.

Keywords: Clostridium Cancer Tumor Cancer-fighting bacteria Bacterial therapy

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Co-culture of SHED-MSCs and inflammatory M1 macrophages alters the TAC and MDA levels as an oxidative stress index (Research Paper)

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Introduction: In inflammatory situations, SHED-MSCs exhibit properties that can modulate the immune response. These cells interact with various types of immune cells, including naïve or M1 macrophages. We believe that when SHED-MSCs are co-cultured with M1 macrophages, it may have an impact on oxidative stress markers such as total antioxidant capacity (TAC) and malondialdehyde (MDA), a peroxidation product. To examine the connection between TAC and MDA as biomarkers for oxidative stress in the supernatant of co-cultured SHED-MSCs and M1 macrophage cells.

Methods: The differentiation of the THP-1 monocyte cell line resulted in the formation of M1 macrophage cells. Once confirmed through flow cytometry, these cells were co-cultured with SHED-MSCs in a trans-well system. The levels of TAC and MDA in the supernatant were then measured using FRAP and TBARS methods, respectively.

Results: In the co-cultures supernatant, the average TAC levels in M1/SHED-MSCs were significantly higher compared to the control group. On the other hand, the average MDA concentrations in the co-cultures supernatant were lower compared to those of controls.

Conclusion: SHED-MSCs have the ability to alter oxidative stress indicators through their interaction with M1 macrophages. This indicates that SHED-MSCs have the ability to alter inflammation markers and modulate the inflammatory condition.

Keywords: SHED-MSCs; Co-culture; Modulate; M1 Macrophages; TAC; MDA

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Co-culture of SHED-MSCs with M0 macrophages changes oxidative stress levels (Research Paper)

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Introduction: SHED-MSCs modulate the immune response by interacting with many immune cells, such as naïve or M0 macrophages. Since M0 macrophages can play an important role in inflammation and can modify important components of the microenvironment, we hypothesized that the co-culture of SHED-MSCs and M0 macrophages could increase antioxidant capacity (TAC) and reduce peroxide products such as malondialdehyde (MDA) as indices of oxidative stress and sensitive markers of inflammation.

Methods: The effect of SHED-MSCs was evaluated by co-culture with THP-1-derived M0 cells, TAC levels by FRAP analysis, and MDA levels by TBAR methods in supernatant co-culture.

Results: Mean TAC levels in the co-culture supernatant were found to be significantly higher compared to the control supernatant mean. The mean levels of MDA were significantly reduced in the co-cultured supernatant compared to the mean of the control or untreated supernatant.

Conclusion: As suggested by our study, SHED-MSCs have the ability to alter indices of oxidative stress and modulate inflammatory conditions

Keywords: SHED-MSCs; Immunomodulatory; Inflammation; Macrophages

Cognitive Neuroscience: Unveiling the Mysteries of the Mind (Review)

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Introduction: Cognitive neuroscience is a multidisciplinary field that aims to understand the complex relationship between the brain and cognitive processes. This article provides an overview of cognitive neuroscience, highlighting its significance in unraveling the mysteries of the human mind. Key topics covered include cognitive methods, brain imaging techniques, and the latest research findings in the field. This article aims to contribute to the academic congress by presenting a comprehensive summary of cognitive neuroscience research and its implications. The human brain, with its intricate neural networks, holds the key to understanding our thoughts, emotions, and behaviors. Cognitive neuroscience combines principles from psychology, neuroscience, and computer science to investigate the neural mechanisms underlying cognitive processes. By studying brain activity, connectivity, and structure, cognitive neuroscientists strive to unveil the fundamental principles that govern cognition.

Methods: Cognitive Methods: Cognitive neuroscience employs a variety of methods to investigate cognitive processes. Experimental techniques such as behavioral paradigms, electroencephalography (EEG), and transcranial magnetic stimulation (TMS) provide insights into cognitive functions at different levels. These methods allow researchers to measure brain activity, assess attention, memory, perception, and language processing, and investigate the effects of cognitive interventions. Brain Imaging Techniques: Brain imaging has revolutionized cognitive neuroscience by enabling non-invasive observation of brain activity. Functional magnetic resonance imaging (fMRI) measures changes in blood oxygenation to infer neural activity and identify brain regions associated with specific cognitive tasks. Diffusion tensor imaging (DTI) provides information about the structural connectivity of the brain's white matter tracts. These techniques, combined with sophisticated data analysis, allow researchers to map brain networks and investigate functional and structural connectivity.

Results: Recent studies in cognitive neuroscience have provided valuable insights into various cognitive processes. For instance, investigations into attentional mechanisms have revealed the brain regions involved in selective attention and the modulation of attentional resources. Studies on memory formation and retrieval have shed light on the hippocampus and its role in

episodic memory. Furthermore, research on language processing has identified specialized brain regions responsible for language comprehension and production. Cognitive neuroscience continues to advance rapidly, driven by technological advancements and interdisciplinary collaborations. Future research aims to explore more complex cognitive processes, such as decision-making and social cognition, and investigate the neural basis of neurological and psychiatric disorders. Additionally, the integration of computational modeling and machine learning techniques holds promise for uncovering the underlying principles of cognition.

Conclusion: Cognitive neuroscience is an evolving field that bridges the gap between the brain and the mind. Through the use of cognitive methods and brain imaging techniques, researchers have made significant strides in understanding the neural mechanisms underlying cognition. This article has provided an overview of cognitive neuroscience, highlighting the importance of this field in unraveling the mysteries of the human mind. By fostering collaborations and utilizing cutting-edge methodologies, cognitive neuroscience holds great potential for further discoveries that will shape our understanding of cognition and its disorders.

Keywords: Cognitive neuroscience, brain imaging, cognition, neural networks, functional connectivity

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Collagen Extraction from Marine Organisms and Its Effect on the Wound Healing Process: A Systematic Review (Review)

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Introduction: Collagen is the main component of the extracellular matrix and plays a crucial role in the wound healing process. However, traditional sources of collagen, such as bovine and porcine sources, have several limitations, including the risk of transmitting diseases and ethical concerns. Marine organisms, such as fish and crustaceans, have become an attractive alternative source of collagen due to their abundance and low risk of disease transmission. This systematic review aims to evaluate the effectiveness of collagen extracted from marine organisms in promoting wound healing.

Methods: A comprehensive literature search was performed using Google Scholar database. The search strategy included keywords ["marine collagen" or "fish collagen" or "crustacean collagen" or "jellyfish collagen" or "sea cucumber collagen" or "starfish collagen"] and "wound" in title. Only studies published between 2012 and 2022 were included in this review.

Results: A total of 22 studies were included in this review. The studies investigated the effects of marine collagen on wound healing both in vitro and in vivo. The results showed that marine collagen has several beneficial effects on the wound healing process, including promoting cell proliferation, improving collagen synthesis, and accelerating wound closure. Moreover, marine collagen was found to have antibacterial properties, which could help prevent infections in wounds.

Conclusion: The findings of this systematic review suggest that collagen extracted from marine organisms has potential as an effective wound healing agent. Marine collagen has several advantages over traditional sources of collagen, including low risk of disease transmission and ethical concerns. However, further research is needed to optimize the extraction and purification of marine collagen and to evaluate its safety and efficacy in clinical studies.

Keywords: collagen; wound; marine organisms; jellyfish

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Combination effect of Cis-platin and selenium nanoparticles on cytotoxicity and apoptotsis against colon cancer (HT29) cell line and evaluation of caspase 8 and 9 genes expression (Research Paper)

amirhossein saadati,[1,*] ghazal kakavand,[2]

1.
2.

Introduction: The use of chemotherapy drugs, along with its benefits, can have severe side effects and also cause drug resistance. One of the ways to reduce the required dose of chemotherapy drugs is to use combined treatments. The aim of this research was to evaluate the combined treatment of cisplatin and selenium nanoparticles against HT-29 colon cancer cells.

Methods: HT-29 cell line was obtained from Tehran Pasteur Institute cell bank and cultured in RPMI1640 medium. Cells were treated with different concentrations of cisplatin, selenium nanoparticles and the combination of both and their survival was evaluated after 24 hours using MTT test. Also, the expression of caspase 8 and 9 genes in the studied cells under the combined treatment of selenium nanoparticles and cisplatin was investigated using real time PCR method. Finally, the percentage of apoptosis in the cells treated with the mentioned compounds was measured using the flow cytometry method and the Annexin/PI kit. The obtained data were analyzed using SPSS software.

Results: The results showed that the IC50 values for cisplatin, selenium nanoparticles, and the combination of cisplatin and selenium nanoparticles were 51, 75 , and 2.9 µg/ml, respectively, which indicates that their combination is more cytotoxic against HT-29 cancer cells. On the other hand, the expression of caspase 8 and 9 genes under the influence of selenium and cisplatin nanoparticles was significantly increased in treated cells ($P<0.05$). Flow cytometry evaluation showed that the number of apoptotic cells increases significantly after the combined treatment of selenium nanoparticles and cisplatin. It was observed that cells with early apoptosis increased by 25.04% and cells with delayed apoptosis by 19.10%.

Conclusion: The results of the present research show that selenium nanoparticles can be used alongside the anticancer drug, cisplatin, and in addition to reducing the required dose of the drug, it increases the efficiency of the treatment and induces apoptosis in HT-29 cancer cells.

Keywords: colon cancer, cisplatin, selenium nanoparticles, apoptosis

Combination of cancer immunotherapies involving CD47/SIRPα inhibition for the treatment of melanoma: a systematic review of animal studies (Review)

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Introduction: Originating in melanocytes, melanoma remains a formidable challenge in clinical oncology, demanding innovative therapeutic approaches to enhance treatment outcomes. Over the past decade, emerging research has spotlighted the potential of targeting CD47 as a promising strategy in cancer therapy. CD47, a cell surface protein, plays a pivotal role in immune evasion and self-tolerance maintenance by transmitting anti-phagocytic signals. Recent studies suggest that the overexpression of CD47 on cancer cells can serve as a "do not eat me" signal to evade phagocytic clearance. SIRPα, a receptor expressed on the surface of macrophages, also plays a crucial role in mediating the same signal in cancer cells through its interaction with CD47. Inhibition of the CD47/SIRPα axis has shown promising effects in melanoma research by promoting macrophage-mediated phagocytosis of tumor cells, potentially enhancing anti-tumor immune responses and affecting the tumor immune escape and therapeutic resistance. Recent studies have proposed a synergistic potential for combining CD47/SIRPα-targeting therapies with other immunotherapy strategies. We aim to review the evolving landscape of CD47/SIRPα targeting combination therapies for the treatment of melanoma.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline was followed to conduct this study. A systematic literature search was conducted in Medline (via PubMed), Scopus, Web of Science, and the Cochrane Library databases with no limit in time and language until August 2023. The search strategy was developed using a proper combination of MeSH terms and free keywords representing CD47, SIRPα, melanoma, and their equivalents. The results were screened for relevance by title/abstract and full-text article, and all animal studies with at

least one arm of CD47/SIRPα-targeting intervention combined with other immunotherapy treatments, were included. Studies of CD47/SIRPα-targeting monotherapies were excluded. Conference proceedings, clinical studies, and reviews were also excluded. The included records were critically appraised for methodological quality by two independent contributors, using the JBI critical appraisal tools, and the points of disagreement were referred to a third contributor. Two independent contributors extracted all relevant data using a standardized data extraction tool.

Results: From a total of 505 search results, six studies meeting the inclusion and exclusion criteria were included in this review. Five studies were conducted by implanting B16-F10 cells in C57BL/6 mice, while one used A375 melanoma NOG mice. Immune checkpoint inhibitors were part of the combined approach in all included studies, with the PD-1/PD-L1 axis as the adjuvant target in four and CTLA-4 in two studies. A4 (anti-mouse CD47 nanobody) was the most common CD47/SIRPα-targeting agent. Inhibited tumor growth was observed among all studies, and three studies reported improved survival. PD-1/PD-L1 combination also showed a durable and lasting immune memory response. Meanwhile, one study combining A4 with αCTLA-4 antibodies and an autologous GM-CSF–secreting tumor vaccine (GVAX) resulted in considerable toxicity.

Conclusion: Our systematic review of animal studies investigating the combination of cancer immunotherapies involving CD47/SIRPα inhibition for the treatment of melanoma underscores the synergistic potential of this approach. The combination of CD47/SIRPα-targeting agents and other immunotherapy strategies seems to provide an effective and comprehensive treatment for melanoma; however, more studies combining CD47/SIRPα axis inhibition with other immunotherapies and conventional cancer treatments, such as chemotherapy and radiotherapy, are required. Undoubtedly, the ultimate decision about the effectiveness and safety of this approach depends on the results of future clinical studies.

Keywords: CD47; Melanoma; Phagocytosis; SIRPα; Systematic review

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Combination of cisplatin treatment and photodynamic therapy attenuates cisplatin-induced cell toxicity in A2780 and A2780-CP cervical cancer cell lines (Research Paper)

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Introduction: Cervical cancer is recognized as a serious worldwide health problem. Despite various achievements for cervical cancer treatment, there are still shortcomings that lead to severe side effects. Combination therapy is fast becoming a key and promising treatment strategy, diminishing chemotherapy-mediated side effects. The objective of this study was to determine the effect of combined cisplatin treatment and photodynamic therapy (PDT) on the cervical cancer recovery.

Methods: In this study, A2780 and A2780-CP cell lines were cultured in the Dulbecco's modified eagle medium (DMEM) enriched with 10% FBS and 1% antibiotic. Both cell lines were treated with cisplatin, photodynamic light (laser with methylene blue as a photosensitizer agent), and the combination of cisplatin treatment and PDT. Half maximum inhibitory concentration (IC50) was calculated for each treatment by the use of tetrazolium salt assay. Both cell lines were examined for cell membrane lipid peroxidation rate

Results: Our findings showed that combination of cisplatin treatment and photodynamic therapy leads to two-fold decreased cisplatin IC50. Results showed that cisplatin and photodynamic light combination could effectively reduce A2780 and A2780-CP cell viability (p-value < 0.0001).

Conclusion: Moreover, combined cisplatin and photodynamic therapy results revealed significantly increased cancer cell membrane destruction through increased lipid peroxidation, resulting in surged MDA content. Our conclusion is that combination of cisplatin and photodynamic therapy can be used as an effective and convenient treatment strategy without considerable side effects.

Keywords: Cervical cancer; Cisplatin; Malondialdehyde; Photodynamic therapy (PDT); Photosensitizer.

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Combination of nanoparticle and stem cell therapy for the management of stroke (Review)

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Introduction: Stroke is currently one of the primary causes of morbidity and mortality worldwide. Unfortunately, the available treatments for stroke are still extremely limited. Indeed, stem cell (SC) therapy is a new option for the treatment of stroke that could significantly expand the therapeutic time window of stroke.

Methods: Some proposed mechanisms for stroke-based SC therapy are the incorporation of SCs into the host brain to replace dead or damaged cells/tissues. Moreover, acute cell delivery can inhibit apoptosis and decrease lesion size, providing immunomudolatory and neuroprotection effects. However, several major SC problems related to SCs such as homing, viability, uncontrolled differentiation, and possible immune response, have limited SC therapy. A combination of SC therapy with nanoparticles (NPs) can be a solution to address these challenges.

Results: NPs have received considerable attention in regulating and controlling the behavior of SCs because of their unique physicochemical properties.

Conclusion: By reviewing the pathophysiology of stroke and the therapeutic benefits of SCs and NPs, we hypothesize that combined therapy will offer a promising future in the field of stroke management. In this work, we discuss recent literature in the SC research combined with NP-based strategies that may have a synergistic outcome after stroke incidence.

Keywords: Stroke; blood-brain barrier (BBB); central nervous system; nanoparticle; stem cell therapy

combining of chemotherapy with stem cell therapy for cervical cancer treatment (Research Paper)

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Introduction: Cervical cancer is the fourth most common cancer in women worldwide and is commonly treated with chemotherapy. However, drug resistance and adverse side effects limit the effectiveness of chemotherapy, highlighting the need for alternative or complementary therapies. This study examined the potential of conditioned medium derived from human amniotic epithelial stem cells (hAEC-CM) as an adjunct therapy to Paclitaxel in treating cervical cancer.

Methods: Human-term placentas were gained from uncomplicated Cesarean sections from healthy donor women. The amnion was peeled from the chorion, and the epithelial stem cells were isolated, cultured, and their conditioned medium was collected. First, the effect of hAEC-CM on cervical cancer cells was evaluated. Then, the cell growth inhibition effect of different concentrations of Paclitaxel on HeLa cervical cancer cells was examined, and subsequently, the combination of hAEC-CM and Paclitaxel was tested. The MTT assay detected the cell viability of cells treated with Paclitaxel, hAEC-CM, and in the combination group.

Results: Our results showed that hAEC-CM alone had a moderate inhibitory effect on HeLa cells, while Paclitaxel alone had a dose-dependent cytotoxic effect. Notably, the combination of hAEC-CM and Paclitaxel led to a significant reduction in the IC50 of Paclitaxel, indicating a potential synergistic effect.

Conclusion: The findings suggest the potential of hAEC-CM as a complementary therapy for Paclitaxel in the treatment of cervical cancer. Further studies are needed to elucidate the underlying mechanisms of this synergistic effect and to explore the clinical potential of this combination therapy.

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Keywords: Cervical cancer, Paclitaxel, Epithelial stem cell, Human amniotic membrane, Proliferation

Comparative Molecular Docking Analysis of Evobrutinib and Orelabrutinib targeting BTK in Multiple Sclerosis (Research Paper)

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Introduction: Multiple Sclerosis (MS) is a chronic autoimmune disease in relation with the central nervous system (CNS). It's believed that cells from either innate or adaptive immune pathways are in charge of the development and progression of the disease. The Bruton's tyrosine kinase (BTK) is a key enzyme, being present in many cells, has been recognized as a potential target for MS treatment. In fact, BTK has a pivotal role in activating immune cells, particularly glial cells and B cells, causing the production of pro-inflammatory cytokines. Extensive studies have indicated that BTK inhibitors can both modulate B-cell function, in order to reduce inflammation and autoantibody production, and regulate immunomodulatory effects of glial cells, including astrocytes and microglia. Moreover, BTK inhibitors have shown promising outcomes in preclinical studies by decreasing demyelination, which is another hallmark in MS pathogenesis. The purpose of this study is to compare the effect of two selective BTK inhibitor, Evobrutinib and Orelabrutinib, on BTK activity. May this survey shed light on the exploration of novel therapeutic agents for the treatment of MS.

Methods: In this research, at first, the BTK structure was downloaded from the Uniprot website, then necessary preparations, including adding charge and hydrogen ions, were performed using Chimera software. The three-dimensional structures of Evobrutinib and Orelabrutinib were obtained from the PubChem website. The binding site of the BTK was determined using Deepsite. [Center; X: 8.1341, Y: 14.500, Z: 36.303 and Dimensions (Angstrom); X, Y, Z: 25.00] Finally, the molecular docking process was operated using AutoDock Vina in PyRx 0.8 to investigate the binding status of Evobrutinib and Orelabrutinib to BTK.

Results: Following the completion of the docking process of Evobrutinib and Orelabrutinib with BTK, using PyRx software, the achieved results are summarized below. For each Model, the data represents their binding affinity, RMSD lower bond and RMSD upper bound, respectively: Evobrutinib: Model #1: [-5.7, 0.0, 0.0] Model #2: [-5.5, 0.0, 0.0] Model #3: [-5.4, 1.603, 2.237] Orelabrutinib: Model #1: [-5.2, 0.0, 0.0] Model #2: [-4.7, 24.23, 26.577] Model #3: [-4.6, 4.434, 6.022]

Conclusion: Based on the findings from the molecular docking analysis of Evobrutinib and Orelabrutinib with BTK, it has been determined that both drugs exhibit negative binding energy. Furthermore, Evobrutinib demonstrated a greater affinity in comparison with Orelabrutinib. Given the data presented in this research, is more likely that Evobrutinib holds promise as a potential treatment option for MS when compared to Orelabrutinib; nevertheless, additional investigation is still needed regarding BTK inhibitors.

Keywords: BTK inhibitor, Multiple Sclerosis, Evobrutinib, Orelabrutinib, Molecular docking

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Comparative study of the effect of dried extract of Citrullus colocynthis in the form of ointment in type 2 diabetes compared to metformin. (Research Paper)

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Introduction: Citrullus colocynthis Aboljahl watermelon with the scientific name Citrullus colocynthis is one of the medicinal plants that have been used by humans since the beginning of time, especially in the geographical location of Iran, and genetically, they are one of the most diverse genetic groups among their family groups1. Genetically, it is very diverse and it is extremely resistant in hot and dry regions2 and it is also extremely sensitive to cold and it is in the same family as gourd, cucumber and gourd4. Iran, Sudan, Arabia have more biological distribution than other places 6. This medicinal plant is used in many diseases such as rheumatism, asthma, leprosy, joint pain, some cancers, and in some cases skin inflammations. The abundance of this plant is the highest in the deserts of Pakistan. In terms of the composition of this type of fruit, the plant has many biocompounds, including glycosides, alkaloids, carbohydrates, and flamoids7, which can be attributed to the therapeutic effect of this plant. Type 2 diabetes: This type of diabetes is a type of physical disorder that occurs with the occurrence of hyperglycemia, one of the risk factors of which is obesity, which is called immobility. Due to the lack of sufficient metabolism, the blood glucose level rises and the body is unable to regulate blood sugar through metabolism. 9 and this type of diabetes can cause many problems, including blindness and amputation. 10 On the other hand, despite the lack of knowledge of the people about this disease, temporary and non-scientific treatments have also fueled the increase of this type of disease. and increase the number of type 2 diabetes all over the world 11. Type 2 diabetes may remain asymptomatic in the body for years, and if the necessary conditions arise to induce itself into the body, it will start to work due to one of the risk factors12. and the cause of tooth decay, severe weakness of body mass, and these factors cause It is possible that the muscles of the person suffering from this disease gradually become atrophied 13 and the body of the affected person becomes weak 14. According to one of the native uses of this type of berley fruit, reducing diabetes in people with type 2 diabetes, in this research, an attempt is made to create a low-risk, easy-to-use alternative to metformin tablets in the form of an ointment, and the result Let's check

Methods: First, 30 male rats were injected intraperitoneally with streptozotocin solution from Sigma company for 10 days in the amount of 0.5cc to all rats, and after 15 days, they were diagnosed by measuring their glucose levels. Using 30 male mice of the breed with a weight of about 250 to 300 grams, they were selected and divided into three groups. Group A only received ointment with a concentration of 20%. The second group or group B received ointment with a concentration of 40%, and group C received metformin tablet solution in the form of 3cc of a saturated solution of metformin tablets. The desired amount to confirm the infection. In rats, blood glucose was 150 or higher. To prepare these concentrations, 20 g of Abu Jahl watermelon dry extract was mixed from 80 g of cold gram, and 60 g of cold gram and 40 g of dried extract of this fruit were used for 40% concentration. Preparation of extract: To prepare the concentrated extract, the extracting process was carried out in 8 hours using a soxole machine and hydroalcoholic solvent. In the next step, the obtained extract was concentrated with the help of a rotary evaporator and stored in a dark place away from sunlight for 24 hours. We set it for an hour, then with the help of a freeze dryer, the concentrated extract was turned into extract powder. Preparation of metformin solution: 5 ml of distilled water was poured into the test tubes and after measuring, one metformin 500 tablet was poured into each of the tubes and mixed with a laboratory shaker until a cloudy solution was obtained. Preparation of ointments: To prepare the ointments, we mixed the extract powder using cold cream in 100 gr packages and stirred well to obtain a homogeneous mixture. After confirming the diabetes of the mice, the treatment process was started on the 15th day. And this treatment was done in the morning and in the evening, for the ointment in the lumbar area, it was first shaved with a razor and the ointment was applied to this place twice a day, and the results were measured and analyzed for ten days.

Results: During the research process, the blood glucose of the rats was measured daily and the results are shown in the following tables. According to the figures obtained from these graphs, the 40% ointment performed better than the 20% ointment and was able to create a proportional downward trend in the blood glucose level of the rats, but considering that this type of use of the proposed medicine It is topical and easy to use, and its slight difference with metformin, which is one of the main drugs in the treatment of diabetes, can be expected that the extract of this plant can be used as a glucose reducer in people with diabetes or temporary hyperglycemia. .

Conclusion: In a research conducted by Rahman et al. in 2020, the anti-diabetic effect of this fruit ointment on diabetes in rats was confirmed15 and also in 2022, the lipid factors and useful alkaloids of this plant were

investigated on diabetes and its influence. It was confirmed 16. In 2020, in a research on the fruit of this plant, they were able to confirm the high antioxidant and anti-diabetic properties of this fruit. 17. In 2022, Mahmoud et al. They confirmed 18. According to the research done, it can be concluded that this fruit can be used as a blood sugar reducing agent even topically, but it cannot be considered as a substitute for the main drugs for the treatment of this disease, the reason can be that in people who have hyperglycemia and their blood glucose level is very high, and the mechanism of reducing blood glucose of this plant is not yet known precisely, it cannot be used as a medicine.

Keywords: Diabetes,, antidiabetic, traditional medicine, medicinal plants, Citrullus colocynthis

Comparative study of the effects of Sertraline and Escitalopram on EGFR protein using molecular docking method (Research Paper)

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Introduction: Glioblastoma is the most malignant of the glial tumors and is associated with extremely poor survival. The majority of GBMs have been identified to harbor genetic events in receptor tyrosine kinase signaling pathways. Among the most relevant pathways are those engaged by activation of epidermal growth factor receptor(EGFR). EGFR amplification is common in GBMs,and together with mutation,rearrangement, and/or altered splicing, genetic alteration of EGFR at large has been observed in 57% of these tumors. Activation of EGFR signaling is triggered by ligand-induced receptor dimerization following which the tyrosine residues presentin the intrinsic kinase domain of one receptor cross-phosphorylate specific residues in the C-terminal tail of the partnering receptor, thus providing a scaffold for the recruitment of effector proteins.Sertraline is a member of tetralins, a secondary amino compound and a dichlorobenzene. Sertraline is a popular antidepressant medication commonly known as a selective serotonin reuptake inhibitor (SSRI).Escitalopram (C20H21FN2O) is a selective serotonin reuptake inhibitor (SSRI) and the S-enantiomer of racemic [citalopram]. It is used to restore serotonergic function in the treatment of depression and anxiety.

Methods: First, we enter the uniprot protein database and search the desired protein, which is EGFR, we select the corresponding human protein from the displayed results. Among the results, we select the protein with more position, less chain and higher resolution. Then we click on the RCSB PDB section and in the next step, we download the desired protein in 3D mode and in PDB format. We also enter the drugs in the Pubchem site and download their 3D mode in SDF format.In order to modify the protein, we enter the Chimera software. We load the EGFR protein into the program in PDB format. We Choose the select section and then choose chain, we can see that the EGFR protein has 5 chains. We compare chains and remove small chains with lower density. In this case, we decided to perform molecular docking on the two larger chains A and B. In the structure section,we check the presence of ions and remove them if existed. At this stage,in the Tools section we apply

changes such as removing solvents, removing non complex ions, adding hydrogen and adding charge. We perform these steps for both A and B chains separately and download the modified protein converted to PDBqt form.After that, we enter the PyRxb software and the load chain A of the modified protein from the load molecule section and apply the make macromolecule option to it.Then we import sertraline and Escitalopram drugs respectively from the import section and choose Minimize all and then convert all to Autodock Ligand option to convert the two drugs from SDF form to PDBqt charged form.Meanwhile, through the deepsite, we find the exact coordinates and active site of each chain.Chain A has the best active site at coordinates [X:103.1 Y:65.8 Z:43.7] and chain B at coordinates [X:63.4 Y:51.8 Z:54.7].We go back to PyRx software, select Vina Wizard, click on start, press Forward in the next step, and in this section manually enter the coordinates obtained from deepsite and start docking. We perform all these steps for chain B after then we get the docking results.

Results: After performing molecular docking on the A and B chains of EGFR protein and on both drugs We can see that RMSD in all four results is 0 and binding affinity in all results are more negative than -5.Our best binding affinity for chain A and Sertraline is -6.6.Best binding affinity for chain A and Escitalopram is -6.1.Best binding affinity for chain B and Sertraline is -6.3.For chain B and Escitalopram binding affinity is -5.9

Conclusion: These results show that both drugs are successfully bound to EGFR protein, but according to the results, Sertraline can establish a stronger connection, better bind to the EGFR protein and therefore be more effective in the treatment of glioblastoma.

Keywords: EGFR protein, Escitalopram, Sertraline, Glioblastoma

comparing chemotherapy plus Radiotherapy versus Radiotherapy alone in lung cancer (Review)

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Introduction: Lung cancer is one of the most common and deadly cancers. Chemotherapy and radiotherapy are the main treatment modalities for this disease. However, there is still much debate regarding the optimal combination of chemotherapy and radiotherapy. In this paper, we aim to review studies that have compared the effects of chemotherapy plus radiotherapy versus radiotherapy alone for the treatment of non-small cell lung cancer.

Methods: For this systematic review, we will search for studies published up to 2020 in PubMed, Scopus and Web of Science. Included studies should be randomized controlled trials that divided non-small cell lung cancer patients into two groups of chemotherapy plus radiotherapy and radiotherapy alone. The main outcomes assessed will be overall survival and progression-free survival.

Results: Preliminary findings show that chemotherapy plus radiotherapy significantly improves overall survival and progression-free survival compared to radiotherapy alone in patients with non-small cell lung cancer. However, these findings need more thorough statistical verification.

Conclusion: Given the results obtained so far, chemotherapy as an adjunct to radiotherapy appears beneficial for the treatment of non-small cell lung cancer. However, further higher quality studies are required before more definitive conclusions can be made. Future studies should also focus on specific chemotherapy regimens and their timing with radiotherapy.

Keywords: lung cancer, chemoradiotherapy, radiotherapy

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Comparing the effects of betaine and Pulsed Electromagnetic Field on the process of osteogenesis in the presence and absence of osteogenic differentiation medium (Research Paper)

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Introduction: Human adipose mesenchymal stem cells (hAdMSCs) are frequently used in tissue engineering and regenerative medicine. Two secure treatments for bone fracture repair are betaine and pulsed electromagnetic fields (PEMF).

Methods: After receiving written permission, abdominal fat was used to remove mesenchymal stem cells, and flow cytometry was used to verify the stemness of the cells. Cells were cultured in -MEM medium with 10% serum as a negative control, in bone differentiation medium as a positive control, in bone differentiation medium and betaine (BET+OD), in betaine (BET), in the bone differentiation environment and waves (OD+ wave), and cells exposed to waves (wave). In this study, cells were cultured for 14 days (8 hours a day) with a 10 mM dosage of betaine and a sinusoidal electromagnetic field with a frequency of 50 HZ and 1 mT intensity. Alizarin red staining, alkaline phosphatase activity, and cell shape were used to assess osteogenic differentiation following treatment. Real-time PCR was used to assess bone gene expression.

Results: Both quantitative and qualitative alizarin red staining results demonstrated a significant reduction in calcium deposition in the OD+wave and wave groups compared to the positive control group, but no significant difference was seen between the other groups. Additionally, the positive control group demonstrated a much higher level of alkaline phosphatase activity than the negative control group. Comparing the BET, OD+wave, and wave groups to the positive control group, a significant reduction in the amount of calcium deposits was seen. In comparison to the negative control group, there was a considerable increase in the expression of the Runx2 and osteocalcin genes in the positive control group. In comparison to the positive control group, the expression level of these genes in the BET group was considerably lower. In comparison to the positive control group, a significant decrease was also seen in the OD+wave and wave groups.

Conclusion: Osteogenic effects of the osteogenic differentiation medium have decreased when betaine and waves are combined with it, whereas the osteogenic effects of the osteogenic differentiation medium alone have increased.

Keywords: human adipose mesenchymal stem cells, Pulsed Electromagnetic Field, betaine

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Comparison and symmetry of the index finger and ring anthropometric surveys in the genetically deafness female population compared with healthy girls of the Persian living in Mashhad (Research Paper)

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Introduction: Biological Anthropology is a branch of human biology and anthropometry is a branch of biometry which deals with the study of human and so determine anthropometric measurements in medical science can help to diagnose, assess and treat abnormalities and applied to identify ethnic groups and describe characterization.

Methods: In the analytical stud, 120 girls aged 7-11years genetic deaf and 200 girls' normal aged 7-11years in Mashhad city have been examined. The distance between the tip of the finger (ring finger and finger pointing) to the end of the inner surface of both hands was measured by a digital caliper. Data collected with Excel 12007 software and SPSS 16 and Mini Tab 16 software's was processed. The means- ratios 2D:4D finger length were compared. The growth pattern of 2D and 4D finger -Symmetric ratio 2D-4D were compared in normal finger girls and genetic deaf in the left and right hand.

Results: The evaluation growth pattern of 2D finger in normal and genetic deaf girls indicate there is symmetry in two groups of subjects. The evaluation growth pattern of 4D finger in normal and genetic deaf girls indicate there is symmetry in two groups of subjects, except for the aged group of 8-9 years, in which there is a significant difference (0.05%).There is symmetry and in assessment ratio 2D-4D in normal and genetic deaf girls in all groups ratio2D-4D in normal people is more than genetic deaf girls. 2D:4D ratio in the left hand of healthy people compared to the left hand of genetic deaf people in the aged group of 9-10 years and 2D:4D ratio in the right hand of healthy people

compared to the right hand of genetic deaf people in the aged group of 7-8 years and 8-9 years shows that there is a significant difference (0.05).

Conclusion: It seems that by extending similar studies to identical populations of anthropometric body sizes, it is possible to provide an appropriate prognosis for the risk of diseases.

Keywords: Fingers Entropy - Symmetric- ratio 2D-4D- genetic deaf

Comparison of drug transfer in cone and cone-cylinder microneedles (Research Paper)

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Introduction: Today, microneedles (MNs) are widely used for medical applications [1]. They have provided successful results in drug delivery. Improving the performance of MNs requires investigating the effective parameters of designing and manufacturing [3]. Experimental studies are time-consuming and expensive while computer simulation can provide helpful information about various effective parameters with more details and lesser cost [6]. Here, the way of drug diffusion inside a cone and cone-cylinder MN was studied numerically. Currently, due to the small dimensions of MNs and technological limitations, it is not possible to experimentally investigate the drug diffusion inside MN. Simulation makes it possible to model phenomena that are impossible or complex in terms of laboratory and obtain useful information about their effective parameters [8].

Methods: To investigate drug diffusion inside MN, COMSOL software was used to simulate drug transfer as a function of time. 3D geometry of cone and cone-cylinder MN was constructed and then meshed. Grid independence was performed for the computational domains created according to the methods described in previous articles [8]. As seen in Figure 1, the height of the microneedles was 800 µm and their base diameter was 300 µm. The governing equation of the diffusion is: (dc_i)/dt- ∇·〖(D_i ∇c_i)〗_ = R_i. (1) Where c_i is the drug concentration [mol/m3], t is time [s], Di is the diffusion coefficient [m2/s] and Ri is the mass source [mol/(m3.s)]. The side wall of the microneedle that is in contact with the skin is considered as the drug sink. At t=0 s, a uniform concentration of the drug inside the microneedle is considered as c(0)= 2·0×〖10〗^(-4) [mol/m3]. For a sample drug with the diffusion coefficient of D=1·48×〖10〗^(-10) [m2/s], the drug diffusion was simulated over time inside the microneedle applying Transport of Diluted Species under a time-dependent model.

Results: The shape of microneedles 1 and 2 is shown in Figure 1. The result of simulation is demonstrated in Figure 2. The distribution of the drug inside the MNs over time is shown in Figure 2. Initially, there is a uniform concentration of the drug inside the MNs that is shown in red. With the passage of time, the drug is transferred from the side wall of the MNs into the

skin, and the contour of the drug concentration inside the MNs changes. At the end of the drug transfer process, the color of the contour changes to blue, indicating that the drug is completely released from the microneedle. Complete transfer of the drug in the cone MN occurs in 64 seconds and in the cone-cylinder ones after 81 seconds. Both microneedles had the same height and diameter, but due to the geometrical difference, they have different volumes of medicine. To make the responses independent of the volume of the MNs, the drug discharge time divide was by the volume (t/V, here t is time and V is the volume of MN). t/V is the time per unit volume. The value of t/V for cone MN is 1.4 times greater than that of the cone-cylinder. That means drug diffusion inside cone shape is faster than cone-cylinder one. The obtained data shows that in addition to the volume of the drug embedded inside the microneedles, their geometry is effective in the complete release of the drug.

Conclusion: Drug penetration inside the microneedle was simulated for different MN shapes. The results show that in addition to the volume of the drug, the geometric shape of the microneedle is effective in releasing the drug from inside the microneedle. In cases where experimental tests cannot be performed due to the complexity of the process or lack of technology, numerical and computer simulations help in understanding various phenomena.

Keywords: Drug delivery, cone microneedles, cone-cylinder microneedles, Simulation

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Comparison of interferon beta and the combination of interferon beta and atazanavir-ritonavir in moderate cases of COVID-19 (Research Paper)

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Introduction: In 2019, covid-19 emerged as a virus targeted respiratory tract and led to the acute respiratory distress syndrome and death. During its pandemic, investigation on antiviral drugs became one of the important research fields. Several drugs have gone under clinical trials and their efficacy against Covid-19 have been assessed and even some of them were imported into guidelines. Moreover, interferons such as interferon beta are another aspect of treatment of this diseases. Recently, studies showed that Atazanavir-Ritonavir along with interferon beta could be used against covid-19. In this study we aimed to compare the efficacy of this antiviral agent with interferon beta.

Methods: This descriptive cross-sectional study was conducted on patients with moderate respiratory involvement due to covid-19 in Shahid Beheshti hospital in 2020. All of the patients above 18 years old were treated with standard national protocol for Covid-19 and their treatment was followed for 4 weeks. Treatments which had been used by these patients were retrieved from pharmacies and was assessed. Patients were divided to two groups based on their consumable drugs: Patients who used Interferon Beta-1 (with brand name Recigen), patients who used interferon Beta-2(with brand name Ziferon), patients who used interferon in combination with Atazanavir-ritonavir. Then demographic variables including age, sex, duration of fever cessation, duration of hospitalization, need for intubation, mechanical ventilation, duration of hospitalization in ICU, final outcome including death or recovery and underlying disease including diabetes, blood pressure, heart and lung disease were extracted and analyzed.

Results: In this study, 135 patients, 65 men (48.15%) and 70 women (51.85%), with an average age of 51.26±16.85 years participated. 42 of the participants received interferon (31.1%) and 93 (68.9%) received INT/ATV. The body temperature of the patients at the time of admission was 37.23 ± 0.82 and at the time of discharge was 36.54 ± 0.37 degrees Celsius, and the systolic blood pressure was 121.93 ± 17.96 at the time of admission and at the time of discharge it was 123.18 ± 11.73 mm Hg. Diastolic blood pressure was 77.73 ± 10.70 mm Hg at the time of admission and 73.54 ± 10.54 mm Hg at the time of discharge. Blood oxygen saturation of the patients was 95.59±2.11% at the time of admission and 96.6%±2.01% at the time of discharge. The heart rate of the patients was 82.83 ± 14.01 per minute at the time of admission and 75.95 ± 8.75 at the time of discharge. The breathing rate of the patients was 17.73 ± 5.37 per minute at the time of admission and 15.26 ± 1.19 at the time of discharge. The length of hospitalization of the patients was on average 5.97 ± 2.77 days and the length of hospitalization in ICU was 10.4 ± 3.53 days. 49 participants (42.7%) had findings positive for COVID_19 on their chest CT image. PCR results were positive for 90 (60%) patients. There were no cases of intubation among the patients. 5 patients (3.7%) were admitted to ICU and 4 patients (3%) died. In this study, the most common underlying diseases were, respectively, 26 people (19.3%) had diabetes, 24 people (17.8%) had high blood pressure, and 12 people (8.9%) had hyperlipidemia. By examining the age of the patients admitted to the ICU, we find that the age of the two drug groups of patients had a statistically significant difference from each other, and the average age of the patients taking interferon was significantly higher than the other group (P=0.016).). Also, it was shown that there was no significant difference between the gender of the patients of the two medication groups admitted to the ICU (P=0.36). In addition, there was no significant difference between the underlying diseases of 5 patients admitted to ICU (P>0.05). The average length of hospitalization in patients who took INT/ATV drug (5.44±2.45) was significantly lower than the group of patients who took interferon alone (7.14±3.1) (p=0.001). We did not observe any difference between the two drug groups in terms of mortality due to corona virus (P=0.407).

Conclusion: In the conducted study, we found that the length of hospitalization and admission to ICU was shorter in patients in the azatanavir/ritonavir group than in the interferon group. However, the mortality rate was not significantly different between the two groups. Due to the lack of a definitive treatment suitable for each stage of the severity of the disease and also due to the contradictory results of various studies regarding the effectiveness of treatment with interferon or interferon together with azatanavir/ritonavir, more research is needed in this regard to achieve an effective treatment. It is necessary for the disease of COVID_19. It is

recommended that in future studies, patients with different levels of disease severity, larger sample size and investigation on other antiviral drugs are also used.

Keywords: Interferon beta, Ritonavir-Atazanavir, Respiratory symptoms, Covid-19

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Comparison of Proliferating Cell Nuclear Antigen (PCNA) Expression in Nasal Polyp and Chronic Rhinosinusitis (Research Paper)

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Introduction: BACKGROUND AND OBJECTIVE: Chronic rhinosinusitis is a common inflammatory disorder in sinonasal mucosa that could be developed with or without nasal polyps. Cellular proliferation is suggested as a possible mechanism of nasal polyp development. However, conducted studies in this context is so limited. So, the present study's aim is the comparison of Proliferating cell nuclear antigen (PCNA) expression in nasal polyps and chronic rhinosinusitis.

Methods: METHODS: In this cross-sectional study, 70 nasal polyp and 60 chronic rhinosinusitis samples from patients referred to Mostafa Khomeini Hospital, Tehran from 2017 to 2022 were immunohistochemically stained by PCNA marker. The percentage of PCNA nuclear expression was determined in two groups and its association with the type of pathological lesion and the patient's age and sex was analyzed by SPSS statistic software version 24 statistical software (IBM Statistics, United States).

Results: FINDINGS: The mean expression of PCNA in nasal polyp and chronic rhinosinusitis samples was 16.55%±13.66 and 17.58%±12.68 respectively (ranging from 0 to 57% in both groups) however, there was no significant statistical difference between the two groups (p=0.479). No relationship was found between PCNA expression with age and sex in none of chronic rhinosinusitis and nasal polyp groups.

Conclusion: CONCLUSION: Proliferative activity of the nasal epithelial cell is similar in chronic rhinosinusitis with and without nasal polyps and it is considered that the increase of epithelial cell proliferative activity probably has no role in nasal polyp development in patients with chronic rhinosinusitis.

Keywords: Chronic rhinosinusitis, Nasal polyp, PCNA, Proliferating cell nuclear antigen,

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Comparison of the effect of exosomes secreted from stem cells derived from menstrual blood And ginger plant exosomes on apoptosis and migration of ovarian cancer cell line SKOV-3 (Review)

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Introduction: Ovarian cancer is the most common fatal malignancy of the female genital tract, which is often diagnosed in advanced stages. Many different approaches are utilized to treat ovarian cancer, including surgery, radiotherapy, and chemotherapy. Still, due to their unsatisfactory effectiveness, researchers are searching for new strategies to lengthen patients' lives and prevent the adverse effects of earlier therapies. Recently, the utilization of cell therapies has increased for a variety of diseases, including cancers, due to the nature of stem cells. These cells exert their therapeutic effects in a paracrine manner. Exosomes with a diameter of 30 to 100 nanometers and a bilayer lipid membrane as a kind of extracellular vesicles (EVs) are thought to be a new treatment option due to their small size, ability to pass through membranes while protecting the proteins and RNAs inside from degradation, and capacity to transport a variety of substances (1). So they occasionally have lower prices, a higher rate of therapy success, and fewer negative side effects than cell therapy for the patient. On the other hand, ginger is known by its inhibitory effects on cancer through reducing oxidative stress and inducing natural cell death. The active compounds of this plant such as gingerol and shogaol are well able to inhibit the production of inflammatory prostaglandins, nitric oxide inhibitors and even interleukins involved in inflammation and in all stages of tumorogenesis, while it has been documented that ginger extract has anti-cancer properties against malignancies of the colon (2), skin (3), liver, breast (2), prostate (4), endometrium (5) and ovary (6). Fresh fruits, vegetables, and plant seeds can all be used to obtain plant exosomes, one of the extracellular nanovesicles of plants. The aim of this study is to compare the effects of exosomes derived from menstrual blood-derived mesenchymal stem cells (C-Exo) and ginger

plant-derived exosomes (P-Exo) on the migration and apoptosis pathway in ovarian cancer Skov3 cells.

Methods: Ovarian cancer cells of SKOV-3 type were purchased from Enyisto-Pasteur Center of Iran. It was cultured In RPMI1640 medium containing 10% bovine serum (FBS) and 1% biotic ratio. The isolation of C- and P-exosomes from NE-MenSCs conditioned medium and ginger extract, respectively, was. Using the Bradford test, cell growth was made. In order to determine the effective dosage of exosomes for treatment, cell viability was evaluated by methyl thiazole tetrazolium (MTT) assay in 0, 50, 100, 200 and 300 µg/ml concentrations. Skov3 cells were used in the 3rd passage. Following 70% confluence, the C- and P-Exo (50 and 100 µg/ml) was added to DMEM containing 10% FBS and 1% penicillin-streptomycin per well. The cells were incubated for 48 h in standard condition, and then the level of apoptosis and expression level of Bax, Bcl2, MMP2, and MMP9 using Annexin V/PI and real time PCR, respectively.

Results: Exosomes obtained from ginger and MenSCs Increase the survival of skov3 cells in a dose- and time-dependent manner, but the effect of C-Exos has a significant effect on the survival of ovarian cells and increases Bax and Bcl2 gene expression, while decrease the expression of MMP2 and MMP9 genes. As a result, according to the Annexin V/PI assay, C-Exo has a significant effect on the apoptosis of cancer cells.

Conclusion: The results of this study show that C-EXO has time- and dose-dependent inhibitory effect on Skov3 cells, so with further research in the future, this compound can be used to develop anti-ovarian cancer drugs.

Keywords: ovarian cancer cells - SKOV-3 cell line - exosome - mesenchymal stem cells - ginger - apoptosis

Complementary medicine in nausea and vomiting caused by chemotherapy in the elderly, a review study (Review)

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Introduction: Nausea and vomiting caused by chemotherapy is one of the most common side reactions to chemotherapy, nausea and vomiting are associated with side effects such as dehydration, fluid and electrolyte imbalance, malnutrition, anorexia and damage to the esophagus and stomach. Uncontrollable nausea and vomiting due to intolerance of chemotherapy and refusal of treatment by patients can delay the chemotherapy program and reduce the quality of life of patients; Therefore, it is very important to try to reduce the side effects of cancer treatment, especially nausea and vomiting. Considering the side effects and low effect of anti-emetic drugs used for nausea and vomiting caused by chemotherapy, one of the basic and low-risk measures to use is complementary and alternative treatments; Therefore, the purpose of this review is to identify non-pharmacological methods or in other words complementary medicine to reduce chemotherapy nausea and vomiting and to introduce these methods to improve the quality.The life of the elderly with cancer.

Methods: PubMed and Google Scholar databases were used to find related articles. The keywords include vomiting, nausea, complementary and alternative medicine, chemotherapy, finally 10 studies were reviewed during the years 2012 to 2020.

Results: After searching, screening and evaluation, the results showed that measures such as breathing exercises, music along with massage therapy around the eyes and acupuncture significantly reduce nausea and vomiting caused by chemotherapy and affect the functional status of patients. On the other hand, medicinal plants such as Zingiber, Achillea millefolium L, Hypericum perforatum L, Citrus aurantium officinale have successfully treated CINV and it has been shown that Zingiber officinale and peppermint extract

are superior to other compounds. Finally, it was found that ice massage in Negan area, in addition to improving the severity of nausea and vomiting in patients, also had a decreasing effect on the frequency of symptoms.

Conclusion: According to recent research results, complementary medicine causes fewer side effects and reduces treatment costs. It is also more effective, less invasive and more accessible compared to other treatments. Recent studies have also shown the increase in the use of CAM in cancer treatment, which can be considered along with other drug treatments to relieve patients' symptoms and increase the quality of life of cancer patients, especially the elderly.

Keywords: Nausea, vomiting, chemotherapy, complementary therapies

Connective tissue grow factor: from molecular understandings to diseases; Systematic Review (Review)

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Introduction: Connective tissue is one of the most important types of tissues in the body, which holds cells together and allows tissues to stretch. Sometimes, for various reasons due to genetic defects, this tissue suffers from various disorders, which are called genetic connective tissue diseases. Genetic or autoimmune connective tissue disease includes a large number of different disorders that can affect the skin, fat, muscle, joints, tendons, ligaments, bone, cartilage, and even the eyes, blood, and blood vessels. the most well-known these disorders are Marfan and related syndromes, Ehlers-Danlos syndrome and Epidermolysis bullosa. In this study, we intend to review the new findings regarding the identification of genes and molecular findings regarding these diseases.

Methods: The electronic databases of MEDLINE, EMBASE, Scopus and other sources were searched for English articles published through January 2020. Three independent reviewers extracted information regarding study design, results and conclusions for each article.

Results: Our review showed that there are not many studies on the identification of genes related to connective tissue disorders and the available findings are very few. The result of examining the findings of the 5 reviewed articles can be summarized as follows: Studies show a critical role of LH3 in α1α1α2(IV) biosynthesis and suggest that LH3 pathogenic variants might contribute to Gould syndrome. Study findings suggest that SLC39A13 is included in gene panels designed to address deformity and short stature. This approach may lead to more efficient detection PLOD genes encode for procollagen lysyl hydroxylase enzymes (LH/PLOD), a family of proteins essential for collagen biosynthesis. Several mutations affect these genes, causing severe disorders, such as Ehlers-Danlos and Bruck syndrome. Mutations in the PLOD1 gene have been linked to kyphoscoliotic Ehlers–Danlos syndrome, and Mutations in the PLOD2 gene have been linked to

Bruck syndrome in humans. The similarity in cEDS and hEDS phenotype in some patients may lead to inaccurate patient classifications. NGS, with an appropriate multigene panel, showed great potential to assist in the diagnosis of EDS and other connective tissue disorders. NGS provides a platform to analyze a panel of genes known to be related to a specific phenotype in a single test. Through whole-exome sequencing and whole-genome sequencing, it also allows the identification of the responsible mutation(s) in genes not previously associated with the disease. Nevertheless, it is not an absolute method. Using NGS for genomic investigation, we cannot perform some tests, e.g., the null allele test for investigating the well-known mechanism of EDS development. Also, an important drawback of the implementation of next-generation sequencing in genetic diagnostics is the detection of a considerable number of variants of unknown significance (VUSs), especially when analyzing larger gene panels.

Conclusion: Years of investigations showed that Connective tissue disorder are a disorder with a very complex phenotype and highly complicated genotype. The comprehensive mapping of the genetic defects in several connective tissue disorders now allows investigators to address the phenotypic spectrum and natural history of several entities in more detail. This will help to differentiate overlapping phenotypes and redefine confusing clinical classifications. Furthermore, the study of connective tissue disorders has led to many new insights into the assembly and homeostasis of the ECM, including TGFβ signaling, intracellular trafficking, and proper Golgi and mitochondrial functioning.

Keywords: Connective tissue disorder, Ehlers-Danlos, Next generation sequencing (NGS), lysyl hydroxylase 3

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Controlling Dental Biofilms (Review)

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Introduction: Biofilms are known as adhesive microbial structures that form on various surfaces. These structures consist of a population of bacteria, fungi, alginate, and other biological materials that interact with each other and form a layered structure on different surfaces. Dental biofilms are one of the most common types of biofilms that form on teeth and can lead to dental caries and periodontal diseases.

Methods: The formation of dental biofilms is a complex process that involves the interaction between bacteria, saliva, and the tooth surface. The initial attachment of bacteria to the tooth surface is mediated by specific adhesins that bind to receptors on the tooth surface. Once attached, bacteria start to produce extracellular polymeric substances (EPS), which form the matrix of the biofilm. The EPS matrix provides protection for bacteria against antimicrobial agents and host defenses.

Results: Prevention and treatment of dental biofilms are critical for maintaining good oral health. Various methods have been developed to control dental biofilms, including mechanical removal by brushing and flossing, chemical agents such as mouthwashes, and antimicrobial agents such as antibiotics. However, these methods have limitations in terms of efficacy and safety.

Conclusion: New approaches to prevent and treat dental biofilms are needed. One promising approach is the use of natural compounds such as plant extracts and essential oils, which have antimicrobial properties and are safe for oral use. Another approach is the use of probiotics, which can compete with pathogenic bacteria and prevent their colonization. Future research should focus on developing new strategies to prevent and treat dental biofilms.

Keywords: Dental biofilms, prevention, treatment, adhesins, extracellular polymeric substances

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Corynebacterium diphtheriae toxin mechanism (Review)

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Introduction: The symptoms of diphtheriae disease include sore throat , fever , cough , hoarseness , and in severe cases , heart failure , kidney failure and paralysis of arms and legs and the involvement of cervical lymph nodes may cause a profound swollen neck sometimes referred to as a “bull-neck”.Coughing can remove parts of the pseudomembrane, easing the situation of the patient temporarily , and after several fits of coughing , the pseudomembrane might even be removed and healing might be achieved. However , in several cases , obstruction of airways results in suffocation , agony and death of the patient. Corynebacterium diphtheriae produces diphtheria toxin , which is a protein with high toxicity and is produced as a result of bacterial contamination with beta bacteriophage , which contains Tox toxin. The pathogenesis of C.diphtheriae is not well elucidated . The most likely entry portals for nontoxigenic C.diphtheriae.

Methods: diphtheriae are skin lessions or dental caries . In recent years , severe and often fatal systemic disease (which were previously quite rare) caused by nontoxigenic C.diphtheriae have been registered in various countries . Nontoxigenic C.diphtheriae often were found to be associated with cutaneous lesions but can transform into severe clinical symptoms , such as myocarditis , polyneuritis , bacteraemia , septic arthritis and endocarditis , characterized by a high mortality rate reaching over 40% . Among the factors that predispose to the invasive infections caused by nontoxigenic C. diphtheriae occurrence are homelessness , abuse of alcohol and injection drugs and diabetes mellitus , hepatic cirrhosis and dental caries . Furthermore , refugees and foreign travelers constitute population groups that are particularly at risk of nontoxigenic C.diphtheriae infections. The gene sequence analysis indicates that DT is preceded by 25 residues of leader peptide , which is most likely involved in toxin secration . DT is produced as a proenzyme that requires specific activation for its toxic function , either prior to or immediately after binding to a sensitive cell.

Results: immunization with diphtheriae toxoid has been extremely effective , and patients with diphtheriae should be promptly treated with antitoxin to neutralize the circulating diphtheriae toxin.

Conclusion: protective antibody titres and to provide supplementary booster doses if the titres are found to be suboptimal. The cornerstone of treatment of suspected respiratory diphtheriae is early administration of diphtheria antitoxin (DAT), which can prevent life-threatening complications. DAT is currently produced using serum from horses that are hyperimmunized with diphtheria toxoid , and there is a global shortage of equine DAT due to high manufacturing costs and previously low demand . beginning in 1997 , physicians have been able to access an unlicensed DAT product from the CDC through an FDA approved investigational New Drug (IND) protocol for emergency treatment of suspected diphtheria cases . In countries with high anti-diphtheriae vaccination coverage , the disease is very rare , but in some regions of Africa and Asia diphtheriae is still recognized , with thousands of cases reported annually .

Keywords: Corynebacterium diphtheriae infections - respiratory infections - vaccination - treatment

COVID-19 as a potential Epstein-Barr virus associated gastric cancer agent (Review)

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Introduction: Recent studies indicate a decline in CD8+ T lymphocytes in COVID-19 patients implying immunosuppression and reactivation of opportunistic viruses respectively. Epstein-Barr virus (EBV), formerly known as Human gammaherpesvirus 4, is an oppurtunistic double-stranded DNA virus and a causative agent of infectious mononucleosis with a subclinical distribution in 90% to 95% of the world population. EBV-associated gastric cancer (EBVaGC) is a distinct subtype of gastrointestinal cancers in terms of carcinogenesis with characteristic clinical and pathological features, including a male predominance, a proximal location in the stomach, and a lymphoepithelioma-like histology. The goal of this review is to discuss reactivation of EBV subsequent to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and highlight the potential role of the latter in EBVaGC.

Methods: To conduct this research, we studied 15 articles regarding “EBV reactivation”, “COVID-19” and “gastric cancer” on NCBI and Google Scholar. We searched for studies published up to September 2023.

Results: Recent studies indicate that 30% of the COVID-19 patients have evidence of EBV reactivation. Researchers found that the proportion of individuals who were simultaneously positive for EBV early antigen (EA) IgG and viral capsid antigen (VCA) IgG was significantly higher in severe COVID-19 patients (25.3%) than in healthy controls (less than 4.22%). This evidence suggests a potential role of COVID-19 infection in EBVaGC emergence. Recent advances in genome-wide and comprehensive molecular analyses have demonstrated that both genetic and epigenetic alterations contribute to

EBVaGC carcinogenesis. Genetic modifications that are characteristic of EBVaGC comprise frequent mutations in PIK3CA and ARID1A and amplification of JAK2 and PD-L1/L2. Additionally, Global CpG island hypermethylation, which triggers epigenetic silencing of tumor suppressor genes is also a unique feature of EBVaGC and is considered to be crucial for its carcinogenesis. Post-transcriptional gene expression regulation by cellular and EBV-derived microRNAs has also been shown to play a critical role in EBVaGC carcinogenesis. These abnormalities result in significant alterations in gene expression related to cell proliferation, apoptosis, migration, and immune signaling pathways.

Conclusion: Limited data and ambiguity of the EBVaGC encourages generation of novel hypothesis regarding its pathogenesis pathways. As discussed above, Severe COVID-19 makes extensive contribution to EBV reactivation through suppressing immune system. Genetic alterations due to EBV reactivation can stimulate the development of EBVaGC by promoting cell growth and survival in addition to suppressing immune response to tumorigenesis. The study of EBVaGC is a rapidly evolving field; As a result, further studies are encouraged to elevate our understanding of EBVaGC and the potential role of COVID-19 infection in its progression in the years to come.

Keywords: Gastric Cancer, Epstein-Barr virus, COVID-19

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COVID-19 Symptoms and Oral Health Status: An Update (Review)

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Introduction: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the virus responsible for COVID-19 disease, is a newly emerged virus with established effects on various systems such as respiratory, gastrointestinal, and neurological systems. Recently, the relationship between SARS-CoV-2 infection and oral cavity lesions in COVID-19 patients has been appraised. The objective of this research is to analyze the literature on the clinical indications of COVID-19 in the oral cavity and their correlation with oral hygiene.

Methods: English language publications from 2019 up to August 2023 on COVID-19, SARS-CoV-2, oral health, and oral lesions were searched on PubMed. This research included all related original, case-report, and review studies.

Results: There is a significant correlation between COVID-19 and oral health, despite the limited number of studies conducted on the subject. The correlation between COVID-19 symptoms and oral health status cannot be ignored. It is essential to be aware of any changes in your oral health, as it can possibly indicate a COVID-19 infection. Therefore, paying attention to any oral symptoms, such as dry mouth, altered taste, or lesions, is crucial. It is highly recommended to seek medical attention immediately if any of these symptoms appear. Stay vigilant and prioritize your health during these unprecedented times. The cytokines released in COVID-19 patients, such as IL-6, IL-1β, and TNF-α, are pro-inflammatory cytokines found in oral diseases that can cause oral cavity lesions. Patients diagnosed with COVID-19 have most commonly experienced recurrent aphthous-like lesions, herpetic lesions, candidiasis, periodontitis, and periapical periodontitis, which can serve as an early indication of COVID-19. Moreover, the presence of viral entry factors like ACE2 in epithelial cells of the oral mucosa suggests a strong correlation between the salivary viral load and COVID-19 symptoms such as taste loss.

Conclusion: Practitioners and dentists must be vigilant in detecting various lesions in the oral cavity caused by the cytokine storm in COVID-19. These

lesions serve as a crucial early indication of COVID-19. However, discovering various forms of COVID-19 oral lesions necessitates extensive research.

Keywords: COVID-19, SARS-CoV-2, coronavirus disease 2019, Oral Health, oral lesions, oral mucosa, Oral disease

crimean congo hemorrhagic fever virus (Review)

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Introduction: According to studies, it was found that ticks of the Hyaloma genus are the main carrier and reservoir of CCHF. This disease occurs only in humans, but its natural cycle includes wild mammals, livestock, birds and ticks. Although the disease-causing virus is often transmitted by ticks, animal-to- human and human-to-human transmission also occur. The way of transmission of CCHF is through tick bites or contact with blood, carcasses of infected animals and humans (people whose jobs are at risk of this disease). The causative agent of this disease is a single-stranded RNA virus with a negative sense, which is classified in the Nairovirus genus of the Bunyaviridae family. Of course, it should be kept in mind that the resistance of CCHF to heat is low and it can be destroyed by heating and cooking the meat, and also this virus can resist in the body and blood for 10 days and detergents do not destroy CCHF only until Some disable it.

Methods: The basic indicator in the diagnosis of laboratory reports of CCHF is the decrease in the level of platelets and leukocytes. Enzymes such as aspartate aminotransferase, alanine aminotransferase, creatinine phosphokinase and lactate dehydrogenase tend to increase. Prolonged clotting time is checked by prothrombin test and activated partial thromboplastin test. Fibrinogen is reduced, which tends to form a network for connecting platelets and proteins to form a clot. An increase in fibrin degradation products can be observed. Within 5 to 9 days, the laboratory results of surviving patients become normal. The treatment strategy for CCHF consists of two aspects, one is to perform symptomatic treatment to cover the deficiencies that occur due to extensive loss of blood cells, such as blood transfusions, platelets or plasma are given to patients. Hypovolemic patients are given electrolytes. Secondary infections are also considered because there is suppression of the immune system and the person becomes susceptible to other diseases.

Results: Humans are the only known hosts that show clinical symptoms associated with this disease. According to a study, the chance of developing

clinical disease in people carrying the virus was 0.215 to 1 in every 5 infected people. The development of the disease has four stages, including an incubation stage where the virus replicates in the body, a pre- bleeding stage, a bleeding stage and a convalescent stage. The basic indicator in the diagnosis of laboratory reports of CCHF is the decrease in the level of platelets and leukocytes. Enzymes such as aspartate aminotransferase, alanine aminotransferase, creatinine phosphokinase and lactate dehydrogenase tend to increase. Prolonged clotting time is checked by prothrombin test and activated partial thromboplastin test. Fibrinogen is reduced, which tends to form a network for connecting platelets and proteins to form a clot. An increase in fibrin degradation products can be observed. Within 5 to 9 days, the laboratory results of surviving patients become normal.

Conclusion: The treatment strategy for CCHF consists of two aspects, one is to perform symptomatic treatment to cover the deficiencies that occur due to extensive loss of blood cells, such as blood transfusions, platelets or plasma are given to patients. Hypovolemic patients are given electrolytes

Keywords: CCHF , Laboratory,Blood , Electrolytes, Enzymes

Crisper-based methods in the diagnosis of SARS-CoV-2 (Review)

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Introduction: Viral diseases have always been a global concern. Recently, SARS-COV-2 virus has caused a pandemic, leads to death. Because of the high rate of prevalence, the detection of this disease in the early stages is important in the outbreak control. There are some conventional techniques to diagnose this virus. Nucleic acid-based detection (NAD) methods, such as different types of polymerase chain reaction (PCR), loop-mediated isothermal amplification (LAMP), nucleic acid sequence-based amplification (NASBA), etc., have been used for this aim, among them, real time PCR is the gold standard for the detection of the virus. Immunoassays, such as, enzyme-linked immunosorbent assay (ELISA) and chemiluminescent immunoassay are extensively used for the detection of the virus and/or the investigation of the previous exposure to the virus. However, these methods have low specificity (because of the cross-reactivity of antibodies) and sensitivity. Clustered regularly interspaced short palindromic repeats (CRISPR), a part of the acquired immunity system in prokaryotes, is a versatile system which has been exploited in different areas in biology and medicine, including genome editing and nucleic acid detection. Owing to the programmable nature of CRISPR-Cas system, it is a proper option for the development of a rapid, sensitive and specific nucleic acid-based detection method. DETECTR (DNA endonuclease-targeted CRISPR trans reporter) that is based on CRISPR–Cas12, SHERLOCK (specific high-sensitivity enzymatic reporter unlocking), which relies on the collateral cleavage activity of Cas13a, MCCD (multiple cross displacement amplification (MCDA) combined with CRISPRR-Cas12a-based Detection), SENSR (sensitive enzymatic nucleic acid sequence reporter), which is based on CRISPR-Cas13a are some of the developed CRISPR/Cas systems for the detection of the viral agent of COVID-19, SARS-

CoV-2.In this review we are going to discuss about the different CRISPR-based systems for detection of SARS-CoV-2.

Methods: DETECTR SHERLOCK MCCD

Results: Crispr-based detection methods is sensitive, specific, fast and cost effective.

Conclusion: Recently, CRISPR system is widely used in various fields of bacterial typing, genetic engineering and detection of various pathogens. Due to human progress in these fields, this system is used for fast, accurate and cost-effective diagnosis of corona virus from clinical samples.

Keywords: SARS-COV-2, COVID19, CRISPR/Cas system, Detection

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CRISPR, an Innovative Method in Gene Therapy for Cancer (Review)

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Introduction: Cancer is a complex disease characterized by uncontrolled cell growth that leads to tumor formation. Traditional cancer therapies such as chemotherapy and radiation often exhibit limitations in terms of specificity, efficacy, and adverse effects. Gene therapy in cancer treatment is one of the critical issues that has been assessed. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), a revolutionary gene-editing technology, offers unprecedented opportunities for precise and efficient genome modifications. This abstract encompasses an analysis of the current literature on the application of CRISPR in cancer gene therapy.

Methods: The terms “CRISPR and cancer treatment” were searched in PubMed, Science Direct, and Google Scholar, the selected articles were critically evaluated.

Results: The application of CRISPR in gene therapy for cancer has demonstrated significant potential across multiple domains. First, in the context of cancer-associated genes, CRISPR can effectively target and deactivate oncogenes, which promote cancer growth, as well as tumor suppressor genes, which typically prevent cancer development. By inactivating oncogenes, CRISPR can reduce abnormal signaling pathways that drive uncontrolled cell growth and division in cancer cells. Conversely, by restoring the function of mutated or silenced tumor suppressor genes, CRISPR can reinstate the intrinsic ability of the cell to regulate cell growth and prevent tumor formation. Second, by utilizing CRISPR-mediated gene correction, it is feasible to rectify specific genetic mutations that underlie the abnormal behavior of cancer cells. This correction has the potential to restore

normal cellular function and halt the cancerous phenotype. Third, CRISPR has been employed to enhance the immune response against cancer by modifying cancer cells to express antigens that are recognized by the immune system. CRISPR is used to introduce genes encoding specific antigens into cancer cells, including tumor-specific antigens (TSAs) and tumor-associated antigens (TAAs). TSAs are exclusive to cancer cells and ideal targets for the immune system. Moreover, CRISPR offers the potential in overcoming treatment resistance by selectively targeting and disrupting resistance mechanisms in cancer cells. These innovative approaches have shown promising outcomes in preclinical models, offering new avenues for cancer treatment.

Conclusion: CRISPR-based gene therapy with the ability to enhance the immune recognition of cancer cells and circumvent treatment resistance highlights the versatility of CRISPR in combating cancer. However, further research are required to address the safety, delivery challenges and long-term efficacy of this therapy. Despite the current limitations, the application of CRISPR in cancer gene therapy represents a groundbreaking approach that may shape the future of cancer treatments.

Keywords: CRISPR, gene therapy, cancer, oncogenes

CRISPR-Cas9 Technology: A Promising Tool for Anti-Cancer Therapy (Review)

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Introduction: Cancer is one of the critical reasons of human deceases worldwide due to the high mortality rate and severe economic problems. Research has shown that the occurrence, progression, and treatment of tumors are related to gene mutation. So, CRISPR/Cas9 can be used in cancer investigation to modify the genome to survey the mechanisms of tumorigenesis and development. CRISPR/Cas9 has arisen as a dominant approach for producing changes to the genomes, which has broadly been used in numerous cell lines. Creating the cell and animal models by CRISPR/Cas9 set the base for the clinical trials that probably treated cancer.

Methods: This study included peer-reviewed papers from Scopus, PubMed, Web of Science, and ScienceDirect databases from 2020 to 2023.

Results: Recently, a CRISPR–Cas9 genome-targeting system has been developed that does not need viral vectors, allowing hasty and effective insertion of large DNA sequences at specific sites in the genomes of human T cells while preserving cell viability and function. This permits an individual or multiplexed modification of endogenous genes that replaces the endogenous T cell receptor locus with a new TCR that redirects T cells to a tumor antigen. The resulting TCR-engineered T cells precisely recognize tumor antigens and increase anti-tumor cell responses in vitro and in vivo. This study proves that non-viral genome targeting can allow quick and flexible investigational manipulation and therapeutic engineering of human immune cells. CRISPR-Cas9 can also be used to target tumors directly in vivo. Genetic mutations that switch on oncogenes stimulate carcinogenesis, and the expression of these oncogenes is specific to cancer cells. Knocking out these oncogenes via CRISPR-Cas9 is an attractive therapeutic target since it will inhibit cancer

growth. Current instances comprise a lipid nanoparticle (LNP)-based delivery method to disrupt the overexpressed PLK1 (Polo Like Kinase 1) gene and a lentivirus delivery approach to target multiple cancer-specific indels.

Conclusion: Extensive research on CRISPR-Cas9 has allowed scientists to overcome the aggressive tumor microenvironment and produce more products for forthcoming clinical use.

Keywords: CRISPR-Cas9, Cancer Therapy, Immunotherapy

CRISPR/Cas9 Technology in Cardiovascular Diseases (Review)

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Introduction: CRISPR/Cas9 technology is a powerful technique that allows the generation of modified cells and organisms necessary to elucidate gene function and mechanisms in human diseases. CRISPR/Cas9 system has become one of the most popular approaches for genome editing in basic and clinical research because of its flexibility and simplicity. Cardiovascular disorder has been the emphasis of basic and clinical investigations because of its high incidence and high disability rate, immensely affecting patients' quality of life and long-term survival.

Methods: This study included peer-reviewed papers from Scopus, PubMed, Web of Science, and ScienceDirect databases from 2020 to 2023.

Results: CRISPR/Cas9 has increased the understanding of cardiovascular disorders (especially atherosclerosis and ischemia-reperfusion injury), lipid metabolism, and genetic inheritance. The pathogenic mechanism of atherosclerosis is intricate because several factors are involved in the pathogenesis. The lipid deposition process is the initial occurrence and expansion of atherosclerosis. Hyperlipidemia, particularly low-density lipoprotein cholesterol (LDL-C), has been revealed to be the most crucial trigger of atherosclerosis pathogenesis and the independent threat factor of cardiovascular disease. One of the most familiar pro-atherosclerotic genes is PCSK9 (pro-protein convertase subtilisin/kexin type9), a lipid metabolism-related gene. Intended disruption of PCSK9 activity through loss of function mutations can meaningfully decrease circulating LDL-C levels, prevent cardiomyocyte autophagy, and lower the danger of coronary heart disorder. Consequently, PCSK9 is one of the most concerned and likely targets of atherosclerosis gene therapy. CRISPR system is a hopeful way to knock down the PCSK9 gene in the human liver. Using CRISPR editors to knock down PCSK9 in cynomolgus monkeys, the CRISPR editors encouraged a considerable decrease in plasma PCSK9 level (90%) and, consequently, a higher decrease in plasma LDL-C level (60%). Also, in ischemia-reperfusion injury, calcium calmodulin-dependent protein kinase IIδ (CaMKIIδ) is an essential protein. Targeting CaMKIIδ using CRISPR-Cas9 is a viable

intervention to protect the heart tissue from ischemia-reperfusion damage in mouse models. Injecting gene editing reagents soon after ischemia exposure was sufficient for the mice to recover from severe heart damage.

Conclusion: This research showed CRISPR/Cas9 system could be a powerful tool in cardiovascular research and a new strategy for treating cardiovascular diseases.

Keywords: CRISPR/Cas9 Technology, Genome Editing, Cardiovascular Diseases, Atherosclerosis, Ischemia-Reperfusi

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Cryoprotective role of pentoxifylline on proliferation and differentiation of spermatogonial stem cell following transplantation into azoospermic torsion mouse model (Research Paper)

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Introduction: Preserving the spermatogonial stem cells (SSCs) in long periods of time during the treatment of male infertility using stem cell banking systems and transplantation is an important issue. Therefore, this study was conducted to develop an optimal cryopreservation protocol for SSCs using 10 mM pentoxifylline (PTX) as an antioxidant in basal freezing medium.

Methods: Testicular torsion—a mouse model for long-term infertility—was used to transplant fresh SSCs (n = 6), fresh SSCs treated with PTX (n = 6), cryopreserved SSCs with basal freezing medium (n = 6), and cryopreserved SSCs treated with PTX (n = 6). Eight weeks after germ cell transplantation, samples were assessed for proliferation, through evaluation of Ddx4 and Id4 markers, and differentiation via evaluation of C-Kit and Sycp3, Tnp1, Tnp2, and Prm1 markers.

Results: According to morphological and flow cytometry results, SSCs are able to form colonies and express Gfra1, Id4, α6-integrin, and β1-integrin markers. We found positive influence from PTX on proliferative and differentiative markers in SSCs transplanted to azoospermic mice. In the recipient testis, donor SSCs formed spermatogenic colonies and sperm.

Conclusion: Respecting these data, adding pentoxifylline is a practical way to precisely cryopreserve germ cells enriched for SSCs in cryopreservation, and this procedure could become an efficient method to restore fertility in a clinical setup. However, more studies are needed to ensure its safety in the long term.

Keywords: Male infertility · Testicular torsion · Spermatogonial stem cells · Transplantation · Antioxidant ·

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CtDNA, a revolution in the future of cancer diagnosis (Review)

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Introduction: Cancer is the second biggest cause of death after heart disease and it is increasing hugely. According to WHO, this deadly disease killed almost 10 million people in 2020. The crucial point about cancer treatment, is early detection. Today, the most common ways to detect cancer are: CT scan (computerized tomography), MRI (magnetic resonance imaging), ultrasound, mammography, pap smear, PET scan (positron emission tomography) and solid biopsy. Each of them has its pros and cons. Some of them are invasive and harmful for the patients. Some kind of cancers are hardly detectable and these methods are not completely reliable in some cases.

Methods: Circulating tumor DNA (ctDNA) is a single or double stranded DNA fragment, released into the blood by cancerous cells. For using these fragments, a few milliliters of blood is needed and the method is called liquid biopsy. Analyzing these fragments can present a huge amount of information about the tumor. Solid biopsy has some limitations because the majority of tumors in the human body are heterogeneous and it would be difficult to choose the appropriate treatment for them.

Results: CtDNA can show the sites of primary and secondary tumors. It is promising for genotyping and also prognosis. By ctDNA it is possible to monitor genetic mutations, tumor progression, cancer development and treatment process.

Conclusion: In the near future ctDNA can change the patient journey completely and help the experts to choose the best treatments. Hence, it is extremely important to focus on new methods and use them to improve the patients life quality and health care systems.

Keywords: CtDNA, cancer, liquid biopsy, cancer treatment

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Curcumin ameliorates cisplatin-induced pancreas toxicity in diabetic rats (Research Paper)

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Introduction: Cisplatin therapy as the most common potent chemotherapeutic process is accompanied by side effects. Inflammatory mechanisms may play an important role in the pathogenesis of Cisplatin-induced pancreas toxicity in diabetic rats. Curcumin is an orange-yellow polyphenol present in curry spice and has anti-inflammatory and antioxidant effects. The current study was planned to investigate the effect of Curcumin on CP-induced pancreas toxicity in Streptozocin (STZ)- induced diabetic rats.

Methods: A total of 32 normal male rats were chosen and randomly divided into four groups: Group A or control received no treatment, Group B received STZ, Group C received STZ + Cisplatin, and Group D received STZ + Cisplatin + Curcumin. Diabetes was induced by a single intraperitoneal injection of STZ (60 mg/kg). Rats were given one dose of 7 mg/kg Cisplatin intraperitoneally. Curcumin treatment involved one dose of 200 mg/kg Curcumin injection intraperitoneally. Serum and tissue samples were harvested for biochemical, and histopathological investigations. The concentration of Glucose and the Lipase and Catalase activities were determined using the photometric method. The Amylase and glutathione peroxidase enzyme activities were evaluated in a kinetic manner. The levels of IL-1β and IL-6 were measured by ELISA. The contents of MDA and SOD were calculated using a fluorometry assay.

Results: Cisplatin administration in diabetic rats resulted in significantly elevated serum levels of blood Glucose, Amylase and Lipase (P<0.05). Coadministration of Cisplatin and Curcumin had an important reducing effect

on Glucose, amylase and lipase compared to the rats treated with Cisplatin alone (P<0.01). The diabetic rats treated with Cisplatin presented significantly elevated levels of MDA(P<0.01). Curcumin ameliorated the elevated levels of MDA (P<0.01). Moreover, Curcumin-therapy resulted in elevated levels of Superoxide dismutase, Catalase, and Glutathione peroxidase enzyme activities (P<0.05). A noticeable elevation in TNF-α, IL-6, and IL-1β levels was observed following Curcumin administration in diabetic rats (P<0.001). The results of histopathological experiments confirmed the anti-inflammatory and antioxidant effects the Curcumin in diabetic rats.

Conclusion: This study highlights the potential role of Curcumin against Cisplatin-induced toxicity in diabetic rats, exhibited through favourable alterations in biochemical and histological changes as well as a reduction in oxidative stress and cytokine levels.

Keywords: Cisplatin, Streptozocin, Diabetes, Curcumin

Curcumin and aspirin modulate gene expression in colon cancer-bearing Mus musculus: A meta-analysis of RNA-seq data (Research Paper)

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Introduction: Colon cancer is a type of cancer that affects the colon, which is the final part of the digestive tract. It usually begins as a small, noncancerous growth called a polyp that can develop into cancer over time. Colon cancer is often diagnosed through screenings such as colonoscopies and can be treated through surgery, chemotherapy, and radiation therapy. Risk factors for colon cancer include age, family history of colon cancer, certain genetic conditions, a diet high in red and processed meats, lack of physical activity, obesity, smoking, and heavy alcohol use

Methods: data was downloaded from the NCBI Gene Expression Omnibus (GEO) website (GSE102342 and GSE97013). The FPKM data was normalized using the normalizeBetweenArrays() function from the limma package. This function normalizes the data by dividing each gene's expression by the library size of the sample in which it was measured. This helps to account for differences in sequencing depth between samples.

Results: Curcumin is a naturally occurring compound found in the spice turmeric. It has been studied for its anti-inflammatory, antioxidant, and anticancer properties. In relation to cancer, curcumin has shown promise as a potential chemopreventive agent. It has been found to inhibit the growth of cancer cells, induce apoptosis (programmed cell death), and inhibit the formation of blood vessels that supply nutrients to tumors. Curcumin has also been investigated for its ability to enhance the effectiveness of chemotherapy and reduce its side effects

Conclusion: Curcumin has been shown to inhibit the growth of colon cancer cells in vitro and in vivo. Curcumin exerts its anti-cancer effects through a number of pathways, including the inhibition of cell growth, differentiation, and apoptosis. More research is needed to fully understand the potential benefits of curcumin for the treatment of colon cancer.

Keywords: Colon cancer, Gene expression, High throughput RNA-seq, Meta-analyses, Curcumin

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Curcumin modulates miR-148a/MSK1/IRS1 axis to increase the chemosensitivity of CD44-positive prostate cancer cells to paclitaxel (Research Paper)

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Introduction: Prostate cancer (PC) is the most frequent cancer and second most common cause of cancer-related death in men. PC is commonly treated with radiotherapy, chemotherapy, and hormone therapy. Paclitaxel inhibits cancer cell proliferation in PC cells. Paclitaxel can also stop the cell cycle from progressing to the G2/M phase and prevent microtubular depolymerization by binding to free tubulin. However, paclitaxel resistance is a major challenge in advanced PC. Curcumin, a natural antioxidant, has been demonstrated to have cytotoxic effects on cancer stem cells (CSCs). Curcumin also upregulates of tumor suppressor miRNAs such as miR-205, miR-143, and miR-208 while silencing oncomirs such as miR-21, miR-14, and miR-183. The goal of this study is to explore if curcumin can help lower chemoresistance to paclitaxel through the regulation of miR-148a-mediated apoptosis in prostate CSCs.

Methods: drugs and reagents were bought from Sigma-Aldrich(St. Louis, MO, USA). Paclitaxel and curcumin were suspended in RPMI and kept at -20º C. We used mini-MACS to enrich CD44+ CSCs from the PC3 cell line, which was verified by immunocytochemistry. The MTT assay and DAPi labeling were used to determine cell survival. The expression of P-glycoprotein protein (P-gp) and CD44 proteins was determined by immunohistochemistry. Real-time PCR was used to evaluate the regulatory effects of curcumin and paclitaxel on miR-148a and its target genes.

Results: Pre-treatment of CD44+cells with curcumin significantly reduced the IC50 value and increased apoptosis rate in CD44+cells compared to paclitaxel alone. In addition, our results found that the co-treatment of carcumin and paclitaxel attenuated the expression of CD44 and P-gp compared to paclitaxel alone. On other hand, Curcumin and paclitaxel combination also enhaced miR-148a levels and down-regulated the levels of its target genes MSK1 and IRS1.

Conclusion: Curcumin improves the paclitaxel sensitivity in CD44+ prostate cancer cells by raising miR-148a expression and inhibiting MSK1 and IRS1.

Keywords: prostate cancer - cancer stem cells - curcumin - paclitaxel - miR-148a

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Cytomegalovirus and its relationship with HIV (Review)

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Introduction: Herpes viruses are one of the groups of viruses that are double-stranded DNA. This group can make infection in the host body for the whole life. They include viruses like Cytomegalovirus, Epstein-Barr virus, B virus and etc. Among the herpes viruses family, CMV is the largest one . CMV like other viruses can make infection in the host body . CMV infection and its disease are prevalent and common about 36% in 6-11 year olds and about 90% in 80-year-olds. Sometimes the symptoms of CMV infection can be controlled by a powerful immune response therefore the symptoms can be concealed or the symptoms are mild .

Methods: This study was conducted from February 11 to March 18 at the Beast Hospital with 149 HIV-positive patients, including 81 men and 68 women. (Table 1) To perform the test, approximately 10 ml of blood was taken from everyone using a 10-syringe, and after examining IgG by CMV antibody test chemiluminescence by Roche Cobas device, it was found that 65.77% of the studied patients, i.e. 98 people, including 67 men and 31 women were shown CMV IgG positive. (Table 2)

Results: In this study, we examined 149 patients who were previously confirmed HIV-positive to investigate Cytomegalovirus Seroprevalency. These people included 81 men and 68 women, which are shown in the table1 by percentage After taking a blood sample and performing the CMV Antibody chemiluminescence test, we found that 98 of the 149 patients in our study,

that is, 68.77% of the patients, were CMV IgG positive(Table 2), 67 of them were men (44.9%) and 31 were women (20.8%).

Conclusion: The spread of the human immunodeficiency virus (HIV), which spreads sporadically from human to human, was linked in the early 1900s . At one time, gay men came increasingly popular in megacity centers, and advanced and unexplainable safety led to the spread of the contagion around the world in the late 1900s . Two years later, what was reportedly finally known as AIDS, scientists discovered the virus that causes the disease: HIV.

Keywords: HIV / CMV / CMV IgG

Cytoprotective and Genoprotective Effects of Satureja Khuzestanica Essential Oil against Busulfan-Induced Sperm Damage in Adult Male Mice: A Comprehensive Review (Review)

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Introduction: Infertility remains a pressing global issue, with chemotherapy-induced sperm damage being a significant contributor to male infertility. Satureja khuzestanica essential oil (SKEO), derived from an aromatic herb, has garnered increasing attention for its potential cytoprotective and genoprotective properties. This review aims to synthesize and critically evaluate the existing body of literature on the protective effects of SKEO against busulfan-mediated sperm damage and seminiferous tubules destruction in adult male mice.

Methods: A comprehensive literature search was conducted across databases such as PubMed, Scopus, and Web of Science, spanning studies from inception until September 2023. Eligible studies were selected based on their relevance to SKEO, busulfan-induced sperm damage, and male mice models. A systematic analysis of methodologies, including the administration of SKEO, busulfan dosage, treatment duration, and assessment tools, was performed to ensure the quality and comparability of the included studies.

Results: A multitude of studies have explored the impact of SKEO on busulfan-induced sperm damage. Findings consistently demonstrate that SKEO administration exerts cytoprotective effects, ameliorating sperm count reduction, motility impairment, and abnormal morphology caused by busulfan. Moreover, histopathological examinations revealed a marked decrease in seminiferous tubules destruction in SKEO-treated mice. These observations suggest that SKEO possesses the potential to mitigate busulfan-induced testicular toxicity through its antioxidative, anti-apoptotic, and genoprotective mechanisms. Further investigation into the underlying mechanisms revealed that SKEO's protective effects are primarily attributed to its potent antioxidant properties. SKEO effectively scavenges reactive oxygen species (ROS), reducing oxidative stress levels in testicular tissue. This antioxidant activity is closely associated with the preservation of mitochondrial function and the

inhibition of apoptosis in sperm cells. Additionally, studies indicate that SKEO may modulate genes related to DNA damage and repair pathways, contributing to its genoprotective effects against busulfan-induced genotoxicity.

Conclusion: In conclusion, the evidence from the reviewed studies supports the notion that Satureja khuzestanica essential oil holds promise as a therapeutic agent for mitigating busulfan-induced sperm damage and seminiferous tubules destruction in adult male mice. Its cytoprotective and genoprotective effects, primarily mediated through antioxidative and anti-apoptotic mechanisms, make it a compelling candidate for future research and potential clinical applications in the field of male infertility.

Keywords: Satureja khuzestanica essential oil,, cytoprotection, genoprotection, infertility, anti-apoptotic,

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Deep learning-based approaches to the Evaluation of Alzheimer's Neuropathologies in fMRI Data (Review)

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Introduction: Alzheimer's disease (AD) is the most common neurodegenerative disease. Several issues correlate with AD, such as a lack or loss of memory, disorientation, and loss of time comprehension. Recent research suggests that the susceptibility of the human population to AD has increased, and early prediction of AD can help control the symptoms drastically. Functional Magnetic Resonance Imaging (fMRI) is a neuroimaging technique that can distinguish between active and non-active brain regions based on blood flow, also known as the "Blood Oxygen Level Dependent" or "BOLD MRI". On the other hand, the increased use of artificial intelligence, such as deep learning or machine learning algorithms, in conjunction with imaging in the healthcare field has been established significantly. The automation in image analysis such as "classification" has reached its acceptability for early diagnosis in medical imaging. The main objective of this review is to provide the reader with a clear picture of the role of deep-learning algorithms in the prediction of Alzheimer's disease based on fMRI data.

Methods: We searched for the following keywords in the Google Scholar database: "Functional Magnetic Resonance" OR "fMRI" "Deep learning" AND "Alzheimer's disease". We also limited the publication dates of the articles to after 2023 to complete the analysis of the latest literature. The search strategy produced 3170 articles. We excluded irrelevant articles based on title and abstract screening. We included 51 articles reviewed in this study.

Results: We investigated the following parameters: accuracy, classification method, data source, and number of patients included in the articles. Most studies showed a significant percentage of accuracy (84%). The number of patients in this study was between 60-389 patients. Most studies acquired their data from the Alzheimer's Disease Neuroimaging Initiative (ADNI). Almost all studies preprocessed fMRI data before modeling.

Conclusion: In this study, we investigated the correlation between deep learning and fMRI for disease detection. Most studies applied various DNN methods to detect AD at different stages. We reported that most studies showed high accuracy (84%) for AD detection. In addition, most studies have shown that deep learning methods are superior to machine-learning methods. We conclude that deep learning algorithms are important for initial-stage Alzheimer's disease detection.

Keywords: Deep learning, Alzheimer's disease,Functional Magnetic Resonance Imaging

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Delivery of CRISPR/Cas9 for antimicrobial resistance: Review Abstract Articles (Review)

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Introduction: In last decades, antimicrobial drugs have been prescribed to inhibit the growth of bacteria, fungi and viruses. Development of antimicrobial resistance with sub-lethal concentration of antibiotic causes spread of acute and chronic infections. Therefore find the strategies for overcoming microbial resistance, is the key for the purpose of treatment of diseases. CRISPR (Clustered Regularly Interspersed Short Palindromic Repeats)-Cas system is an adaptive immune system of bacteria and archaea. This system has regulatory effect on bacterial pathogenicity. The Cas9 nuclease of the CRISPR-Cas uses RNA-guided endonuclease provided the ability to rapidly and economically introduce sequence-specific modifications depends on the generation of double-strand break (DSB) and DNA repair process into the genomes of cell and organisms. Which means this sequence can be easily replaced by our desired sequence to retarget the CRISPR-cas9 nuclease and breaks antimicrobial resistance. Safe and efficient delivery of CRISPR/Cas9 systems is still a challenge. In this review, we discuss non-viral delivery systems based on nanoparticles for target delivery of CRISPR/Cas9 for Genome Editing.

Methods: CRISPR/Cas system is the most flexible and user-friendly platform for genome editing. Non-viral delivery systems based on nanoparticles are the most widely used method for target delivery of CRISPR/Cas9 for Genome Editing.

Results: Non-viral vectors, including Nano carriers and nanoparticles such as Nano polymeric- and lipid-based structures, rigid nanoparticles, nanoparticles coupled to specific ligand systems including arginine–glycine–aspartate (RGD) peptide, porous silicon, mesoporous silica, metal–organic, cell-penetrating peptides.

Conclusion: Non-viral vectors based on Nano carriers plays an important role for targeting delivery of CRISPR/Cas9 systems due to increase the circulation time, low toxicity, biocompatibility, and facilitating scaled up. The shape, size, and surface chemistry of NPs are the critical factors that regulate nuclear for cellular uptake, bio distribution, and rapid clearance.

Keywords: antimicrobial resistance, CRISPR/Cas9, Genome Editing tools, Nano carriers

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Design and Production of an Engineered Endolysin with Lytic Activity against Methicillin-Resistant Staphylococcus Aureus (Research Paper)

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Introduction: Improper use of antibiotics has alarmingly led to the emergence of antibiotic resistance. Hence, we urgently needed to find a suitable alternative to traditional antibiotics. Endolysins are enzymes produced at the end of the phage replication cycle and destroy the peptidoglycan of the bacterial cell wall leading to the lysis of the host bacterial cell. These enzymes are species-specific, exhibit high lytic activity, and it is almost impossible for bacteria to develop resistance against them. Lysozyme subfamily 2 (LYZ2) is a modular region of the gene 61 (gp61) of phage φMR11 with lytic activity against S. aureus. However, it does not possess a cell wall recognition domain, usually found in lysins acting against gram-positive bacteria. Therefore, we aimed to design a chimeric endolysin capable of specifically targeting and eliminating methicillin-resistant Staphylococcus aureus (MRSA) bacteria.

Methods: In this study, we engineered the LYZ2 by fusing a Staphylococcus aureus cell wall-binding domain (CBD) to its C-terminus and cloned the chimeric protein (named chimeric staphylococcus aureus–targeting enzybiotic (CSTEnz)) into the pET28a vector, and expressed the enzyme in E. coli BL21 (DE3) cell. The antibacterial property of the enzyme was further evaluated by turbidity reduction assay, disk diffusion assay, and antimicrobial susceptibility testing.

Results: The engineered lysin displayed a rapid and specific lytic activity against susceptible and Methicillin-resistant staphylococcus aureus and inhibited the growth of the bacteria at concentrations higher than 0.5 µg/ml. Besides, the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of CSTEnz were 128 and 64 times lower than those of LYZ2, indicating the increased bacteriolytic activity of the engineered version of the enzyme.

Conclusion: In conclusion, the chimeric enzybiotic can be used as a potential antibacterial agent to limit infections caused by methicillin-resistant Staphylococcus aureus.

Keywords: Endolysin, Methicillin-Resistant Staphylococcus aureus, Antibiotic Resistance, Phage, enzyme Engine

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Design of novel inhibitory peptides against SARS-CoV-2 infection by targeting CD147/RBD interaction using computational approaches (Research Paper)

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Introduction: The COVID-19 pandemic has caused many deaths around the world. The appearance of new variants has complicated the eradication of SARS-CoV-2 despite all efforts to control the pandemic. CD147, also known as basigin or EMMPRIN, is a transmembrane glycoprotein that plays a crucial role in many different cancers and is required for entering the SARS-COV2 virus into the host cell. This study aimed to design novel inhibitory peptides against SARS-CoV-2 entry by disturbing CD147 /RBD interaction.

Methods: The three-dimensional structure of CD147 was extracted from the RCSB protein data bank and docked against the RBD. The important residues that participate in the formation of the SARS-CoV-2-CD147 interface were identified. The residues with unfavorable binding energies were chosen as mutation sites. Peptide inhibitors were developed by the mutation of RBD residues in the virus-receptors complex which had unfavorable energies. The final hits were selected from the initial library of peptides by evaluating their affinity for CD147 binding, safety, and allergenicity.

Results: A collection of 48 peptide candidates was created and the binding affinity of each peptide to the CD147 receptor was assessed through molecular docking. Finally, three non-allergenic and toxic inhibitory peptides with the lowest binding score were introduced.

Conclusion: Our results suggest that the designed inhibitory peptides could be promising therapeutic options for preventing COVID-19 infection and targeting various tumor types.

Keywords: CD147, SARS-COV2, COVID-19, RBD

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Design of specific inhibitor against SARS-CoV-2 3Clpro based on 59S ligand structure in 7WO3.pdb crystal structure using virtual screening methods (Research Paper)

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Introduction: After the increase in the cases of SARS-Corona Virus 2019 and the global spread of the COVID-19 disease, the World Health Organization (WHO) announced the outbreak of the new coronavirus as the cause of public health emergency worldwide. Due to the pathogenicity of this virus and the consequences caused by it, the production of effective drugs or vacccines against this viral infection has been intensively considered. Today, one of the most important methods of producing specific drugs against bacterial or viral agents is the use of advanced virtual screening approaches.

Methods: In current study, we decided to use the crystal structures of 7WO3.pdb to propose effective inhibitors to inhibit the replication of the SARS-CoV-2 virus and, as a result, to effectively treat the disease of COVID-19. It seems that finding an inhibitor with suitable binding ability to SARS-CoV-2 3CLpro can lead to finding chemical structures with high ability to inhibit the replication and function of this virus. For this, after performing the validation phase on 59S ligand against SARS-CoV-2 3CLpro in 7WO3.pdb file, 82 chemical structures with structural similarity to 59S was screened from Pubchem data center and separately were docked to SARS-CoV-2 3CLpro coordination from 7WO3 PDB file and finally arranged based on the acquired ΔGbinding. In last step, essential pharmaceutical attributes of the three compounds with lowest ΔGbinding were also predicted using in silico tools.

Results: while the lowest ΔGbinding for 59S ligand was -6.8 kCal/mol, cyclo[Ala-Ala-Ala-N(Me)Tyr(Me)] with ΔGbinding=-8.2 kCal/mol; N-[5-[(3S,6R,9S)-3-butan-2-yl-6-[(4-methoxyphenyl)methyl]-2,5,8,11-tetraoxo-1,4,7,10-tetrazabicyclo[10.4.0]hexadecan-9-yl]pentyl]-N-hydroxyformamide) with ΔGbinding=-8.0 kCal/mol; and N-[5-[(3S,6R,9S,12R)-3-[(2R)-butan-2-yl]-6-[(4-methoxyphenyl)methyl]-2,5,8,11-tetraoxo-1,4,7,10-tetrazabicyclo[10.4.0]hexadecan-9-yl]pentyl]-N-hydroxyacetamide with

ΔGbinding=-8.0 kCal/mol showed the lowest values between all of selected compounds. Also, computational based predicted attributes of the indicated compounds confirmed their potential to may use as efficient medicine.

Conclusion: Meanwhile, the use of virtual screening methods can be considered and used as an efficient and effective method to find strong and specific inhibitors of SARS-CoV-2 3CLpro. Such chemical structures with high affinity to SARS-CoV-2 3CLpro and acceptable pharmaceutical properties that inhibit the replication and function of the SARS-CoV-2 virus can eventually be considered as an option for the efficient and specific treatment of COVID-19.

Keywords: SARS-CoV-2, COVID-19, SARS-CoV-2 3CLpro, Virtual Screening

Designing a Complex to silence DTNBP1 Gene in schizophrenia with CRISPRi meditated Gene repression (Research Paper)

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Introduction: Schizophrenia is a complex biological disorder with multifactorial mode of transmission where non-genetic determinants are also play important role. It is now clear that it involves combined effect of many genes, each conferring a small increase in liability to the illness. Thus no causal disease genes or single gene of major effects, only susceptible genes are operating. Given this complexity, it comes as no surprise of the difficulty to find susceptible genes. However, schizophrenia genes have been found at last. Recent studies on molecular genetics of schizophrenia which focused on positional and functional candidate genes postulated to be associated with schizophrenia are beginning to produce findings of great interest (1). Schizophrenia is a heterogeneous syndrome, affecting ~1% of the population and characterized by debilitating positive, negative, and cognitive symptoms in addition to severe comorbidities. Despite the enormous burden on worldwide health including 1.9–2.8% of total years lived with disability and a 10–20 year reduction in life expectancy, no drugs with novel mechanisms of action have emerged in the last three decades. Current antipsychotic medications only achieve full symptom remission in 15–25% of affected individuals and adverse side-effects such as weight gain, metabolic disturbances, over-sedation, extrapyramidal symptoms, and agranulocytosis are persistent problems (2). These include neuregulin (NRG-1, 8p12–21), dysbindin, (DTNBP1,6p22.3), G72 (13q34), D-amino acid oxidase (DAAO,12q24), proline dehydrogenase (PRODH-2, 22q11.21), catechol-O-methyltransferase (COMT, 22q11.21), regulator of G protein signaling (RGS-4), 5HT2A and dopamine D3 receptor (DRD3)(1). We have investigated the gene for dystrobrevin-binding protein 1 (DTNBP1), or dysbindin, which has been strongly suggested as a positional candidate gene for schizophrenia, in three samples of subjects with schizophrenia and unaffected control subjects of German (418 cases, 285 controls), Polish (294 cases, 113 controls), and Swedish (142 cases, 272 controls) descent. We analyzed five single-nucleotide polymorphisms (P1635, P1325, P1320, P1757, and P1578) and identified significant evidence of association in the Swedish sample but not in those from Germany or Poland. The results in the Swedish sample became even more significant after a separate analysis of those cases with a positive family history of schizophrenia, in whom the five-marker haplotype A-C-A-T-T showed a P value of .00009 (3.1% in controls, 17.8% in cases; OR 6.75;

P=.00153 after Bonferroni correction). Our results suggest that genetic variation in the dysbindin gene is particularly involved in the development of schizophrenia in cases with a familial loading of the disease (3). DTNBP1 (dystrobrevin binding protein 1) is a leading candidate susceptibility gene in schizophrenia and is associated with working memory capacity in normal subjects. In schizophrenia, the encoded protein dystrobrevin-binding protein 1 (dysbindin-1) is often reduced in excitatory cortical limbic synapses. We found that reduced dysbindin-1 in mice yielded deficits in auditory-evoked response adaptation, prepulse inhibition of startle, and evoked γ-activity, similar to patterns in schizophrenia. In contrast to the role of dysbindin-1 in glutamatergic transmission, γ-band abnormalities in schizophrenia are most often attributed to disrupted inhibition and reductions in parvalbumin-positive interneuron (PV cell) activity. To determine the mechanism underlying electrophysiological deficits related to reduced dysbindin-1 and the potential role of PV cells, we examined PV cell immunoreactivity and measured changes in net circuit activity using voltage-sensitive dye imaging. The dominant circuit impact of reduced dysbindin-1 was impaired inhibition, and PV cell immunoreactivity was reduced. Thus, this model provides a link between a validated candidate gene and an auditory endophenotypes. Furthermore, these data implicate reduced fast-phasic inhibition as a common underlying mechanism of schizophrenia-associated intermediate phenotypes (4). Fig.1. Mice with reduced dysbindin-1 expression (Dys−/−) show a prominent loss of inhibition. During imaging of membrane voltage in the hippocampal area CA1 (A), electrical stimulation generates a brief local excitation (red) followed by a hyperpolarization (blue; B). In Dys−/− mice, the dominant impact is loss of inhibition (C). Decay time constant of this response was used to measure the kinetics of repolarization (C Inset). (D) The decay time constant was significantly prolonged in Dys1−/− mice. (E) When the decay time constant from Dys−/− mice is plotted over sigmodal waves representing 80 or 30 Hz, it is clear that it would be more difficult for the CA1 neurons in the Dys−/− mice to generate higher-frequency oscillations (red trace) compared with normal mice (blue trace). Thus, the loss of high γ-activity (60–100 Hz) observed in the Dys−/− mice and characteristic of schizophrenia may be directly caused by reduced fast inhibitory function (4). CRISPR/Cas9 Technology Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) systems and their CRISPR associated proteins (Cas proteins) have allowed for an unprecedented ability to manipulate the genome. Key amongst the applications of these systems is their use in gene editing for targeted gene knockout, knockin, and modification (6). It makes it possible to correct errors in the genome and turn on or off genes in cells and organisms quickly, cheaply and with relative ease. It has a number of laboratory applications including rapid generation of cellular and animal models, functional genomic screens and live imaging of the cellular genome

(7). CRISPR systems exist across a wide range of bacterial species, providing a rich source of functional diversity for genome editing in eukaryotic cells (8,9). The first described, and most commonly used, is the type-II CRISPR-Cas9 system from Streptococcus pyogenes (SpCas9), a DNA endonuclease that is directed to induce double strand breaks (DSBs) at specific genomic loci via a programmable guide RNA (gRNA) molecule that mediates complementary DNA-RNA base pairing. For SpCas9 to efficiently bind and cleave DNA, the target sequence must be flanked on the 3′ side by an 'NGG' protospacer adjacent motif (PAM) sequence (10). Since the initial implementation of CRISPR systems in eukaryotic cells there has been a rapid expansion of variant enzymes that broaden the capabilities of CRISPR-based platforms (9,11). Each has its own set of features and criteria for sequence recognition that provides added flexibility for adaptation as a research or therapeutic tool (12) that are smaller than SpCas9, allowing easier packaging into size-limited delivery vectors such as adenoassociated virus (AAV) (13), while others can catalyse the maturation of their own gRNAs, simplifying the process of target multiplexing (14). Yet another family of Cas enzymes named Cas13 (previously known as C2c2) target RNA instead of DNA, providing an alternative approach to manipulate gene expression (15,16). The Cas9 protein is an endonuclease containing two nuclease domains, RuvC and HNH. The RuvC domain cleaves noncomplementary DNA strands, while the HNH domain cleaves complementary DNA strands. The sgRNA is composed of the trans-activating crRNA (tracrRNA) and crRNA. The crRNA contains a 20-nt protospacer element and an additional sequence that is complementary to the tracrRNA. The tracrRNA hybridizes to the crRNA and binds the Cas9 protein, forming the CRISPR-Cas9/sgRNA complex to create double-stranded breaks (DSBs) at target sites in the genome. The dual-tracrRNA:crRNA is normally engineered as a single-strand sgRNA containing two crucial segments: a duplex RNA structure at the 3′ end to bind Cas9 and a guide sequence at the 5′ end to bind target DNA sequence. this two-component system is simple but powerful. sgRNA recognizes a specific sequence in the genome, and Cas9 acts as a pair of scissors to cleave the DNA sequence (17). A number of challenges remain before the potential of CRISPR/Cas9 can be translated to effective treatments at the bedside. A particular issue is how to deliver gene editing to the right cells, especially if the treatment is to be delivered in vivo. To safely deliver Cas9 encoding genes and guide RNAs in vivo without any associated toxicity, a suitable vector is needed. A smaller Cas9 gene could be used, but this has additional implications on efficacy (7). Fig. 2. Schematic of the RNA-guided Cas9; The Cas9 nuclease from S. pyogenes (in yellow) is targeted to genomic DNA by an sgRNA consisting of a 20-nt guide sequence (blue) and a scaffold (red). The guide sequence pairs with the DNA target (blue bar on top strand), directly upstream of a requisite 5′-NGG adjacent motif (PAM; pink). Cas9 mediates a DSB ~3 bp upstream of

the PAM (red triangle) (18,19). technologies As with other designer nuclease technologies such as ZFNs and TALENs, Cas9 can facilitate targeted DNA DSBs at specific loci of interest in the mammalian genome and stimulate genome editing via NHEJ or HDR. Cas9 offers several potential advantages over ZFNs and TALENs, including the ease of customization, higher targeting efficiency and the ability to facilitate multiplex genome editing. Cas9 can be easily retargeted to new DNA sequences by simply purchasing a pair of oligos encoding the 20-nt guide sequence. In contrast, retargeting of TALEN for a new DNA sequence requires the construction of two new TALEN genes. Although a variety of protocols exist for TALEN construction, it takes substantially more hands -on time to construct a new pair of TALENs. Mutating catalytic residues in either the RuvC or the HNH nuclease domain of SpCas9 converts the enzyme into a DNA nicking enzyme. In contrast, TALENs cleave nonspecifically in the 12–24-bp linker between the pair of TALEN monomer-binding sites (18). dCas9-KRAB Repression The control of gene expression by transcription factor binding sites frequently determines phenotype. However, it has been difficult to assay the function of single transcription factor binding sites within larger transcription networks. CRISPR interference/activation (CRISPRi/a) technology provides a simple and efficient approach for targeted repression or activation of gene expression in the mammalian genome. It is highly flexible and programmable, using an RNA-guided nuclease-deficient Cas9 (dCas9) protein fused with transcriptional regulators for targeting specific genes to effect their regulation. Multiple studies have shown how this method is an effective way to achieve efficient and specific transcriptional repression or activation of single or multiple genes. Sustained transcriptional modulation can be obtained by stable expression of CRISPR components, which enables directed reprogramming of cell fate. Here, we introduce the basics of CRISPRi/a technology for genome repression or activation (A). The expression of genetic material governs brain development, differentiation, and function, and targeted manipulation of gene expression is required to understand contributions of gene function to health and disease states. Although recent improvements in CRISPR/dCas9 interference (CRISPRi) technology have enabled targeted transcriptional repression at selected genomic sites, integrating these techniques for use in non-dividing neuronal systems remains challenging. Here we used a strategy to adapt an improved dCas9-KRAB-MeCP2 repression system for robust transcriptional inhibition in neurons. Next, we demonstrate transcriptional repression using CRISPR sgRNAs targeting diverse gene promoters, and show superiority of this system in neurons compared to existing RNA interference methods for robust transcript specific manipulation at the complex Dystrobrevin Binding Protein 1 (DTNBP1) gene. Our findings advance this improved CRISPRi technology for use in neuronal systems for

the first time, potentially enabling improved ability to manipulate gene expression states in the nervous system (5).

Methods: 10 Oligonucleotides (gRNAs) were designed with Chop-Chop, and we're analized with data's to check the specificity and off Target activity. The gRNA which showed more efficiency results, was further investigated. With the help of the gRNA webserver tool, we were able to show that the selected gRNA has the highest effectiveness rate while the lowest off-target rate is reported. Then, this gRNA was compared to CRISPR/dCas9-KRAB (7540bp) plasmid of AddGene tool to be identified as efficient DTNBP1 gene silencing Complex.

Results: 10 top gRNAs designed for DTNBP1 Gene silencing with Chop-Chop tool. Throughout the analysis, tge Ranked 1 oligonucleotide had been selected for CRISPR complex. List of possible off-targets of our Ranked 1 oligonucleotide. According to further details and analysis, the Highest level of specificity have been reported

Conclusion: The corresponding gRNA with maximum effect and on-target was selected with the help of data analysis. Next, the plasmid related to CRISPR/dCas9-KRAB was selected to target the DTNBP1 gene with the help of AddGene's reviewed results. At the end, gRNA was analyzed by gRNA webserver tool regarding the on/off target ability and Specificity, and finally, the highest level of effectiveness was shown

Keywords: Schizophrenia, DTNBP1, CRISPRi, KRAB

Designing CRISPR to eliminate miR-200c expression in pancreatic beta cells (Research Paper)

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Introduction: The number of people with diabetes between 20 and 79 years of age is expected to reach 642 million by 2040. This is of great concern because the increasing prevalence of diabetes increases the number of chronic and acute diseases in the general population, with profound effects on quality of life, demand for health services, and economic costs. Complications of diabetes, including diseases such as stroke and cardiovascular diseases, such as kidney disease, retinopathy, and neuropathy, are associated with lower limb amputations, and even in diseases such as cancer, aging-related outcomes (e.g., dementia), infections and liver diseases are known to be effective. This is while now 5% of the deaths occurred due to diabetes, which can be said to increase by 50% in the next ten years. Iran also has nearly 6.3 million people with diabetes and about 7.7 million people with glucose tolerance disorders. The most common types of diabetes are type I diabetes and type II diabetes, and the distinctive feature of these two is the death of pancreatic beta cells. Type I diabetes occurs due to auto-immunity and the result is the death of β cells, so the amount of insulin hormone decreases drastically. In type II diabetes this decrease is approximately 50% and the severity is less than type I diabetes. According to the research of Frederick and his colleagues in 2015, removing the expression of mir-200c partially prevents the apoptosis of beta cells. Controlling type I diabetes requires daily and frequent use of the hormone insulin, but type 2 diabetes can be controlled by taking a series of oral drugs effective on beta cells. With all this, diabetes doesn't get the desired result with these treatment methods and people with diabetes have to bear the side effects of these in treatment methods in addition to taking medicine or insulin constantly. Oral medications for diabetes and insulin have many side effects. The inability of such treatments and the reduction of the effect of these drugs in the long term have caused scientists to discover new and more appropriate ways to control diabetes and its complications. Compared to previous genome editing tools, namely ZFNs and TALENs, which used difficult-to-engineer proteins to target and cut genomic

loci, CRISPR is more time- and cost-effective. Therefore, it is hoped that through CRISPR we will be able to achieve a favorable treatment for diabetes.

Methods: In this project, using CRISPOR web software for Mir-200c, I designed a gRNA with NHEJ strategy to knock out Mir-200c and considering NGG as PAM, and meanwhile, I tried to find the best option. With the aim of not having off target and high On target efficiency and making the necessary changes in it. Then I chose the lentiCRISPRv2 (Zhang lab) vector for cloning through the CRISPOR site and the vectors it introduces for gRNA, and then I cloned the gRNA using SnapGen software.

Results: The micro RNA sequence we got from the NCBI site: CCCTCGTCTTACCCAGCAGTGTTTGGGTGCGGTTGGGAGTCTCTAATAC TGCCGGGTAATGATGGAGG Designed gRNA: AAACACTGCTGGGTAAGACGAGG Final designed gRNA: GAAACACTGCTGGGTAAGACG + AGG

Conclusion: In 2016, Chang and his colleagues aimed to investigate the capability of the CRISPR cas9 system in suppressing the expression of microRNAs, through the website https://zlab.bio/guide-design-resources, two numbers of gRNA for each of Mir-200c, Mir17 and Mir141 and with They designed PAM, NGG and also requested the lenti-CRISPR plasmid from Dr. Zhang's laboratory through the Addgene site and as a result of their activity, they observed a 96% decrease in the expression of each of those MicroRNAs. Their gRNA sequences for mir200c, mir17 and mir141 are respectively: 1) 5′-ATACTGCCGGGTAATGATGG-3′ ۵ (۲ و′-CTAATACTGCCGGGTAATGA-3′ 1) 5′-TGTCAAAGTGCTTACAGTGC-3′ (۲ و ۵′-TGAAGGCACTTGTAGCATTA-3′ 1) 5′-TCCATCTTCCAGTACAGTGT-3′ و ۵ (۲′-CTAACACTGTCTGGTAAAGA-3′ They also proved that traditional methods such as antisense inhibitors etc. are not very potential for suppressing the expression of members of a family of miRs due to their conserved sequences. While using the CRISPR system and designing efficient gRNAs, the amount of off-target can be minimized when inhibiting a miR from members of the same family. Another result of their research was that the knock-out effects of CRISPR/CAS9 system on miRs can be stable and long-term. The work done by Chang and his colleagues also proves our work in the following aspects: Mr. Chang and his colleagues started working with CRISPR and designing gRNA with the aim of reducing the expression of mRNAs, which happened to include mir-200c, just like what we did, that is, to remove mir-200c, we used the CRISPR system and gRNA In addition, our work, and their work were also similar in other aspects, such as the selected website for gRNA design (CRISPOR is among the sites introduced in Dr.

Zhang's laboratory), the selection of NGG as PAM, with the difference that the target Ours were different from each other (our goal is to eliminate the expression of mir-200c for the treatment of diabetes in humans, but their goal was only to investigate the effect of CRISPR in reducing the expression of microRNAs) and for this reason, the designed gRNAs are also different because for us, It was important to have high on-target efficiency and low off-target efficiency, and finally, since they have received a 96% response in reducing the expression of miRs under test, then probably our project will also be successful, and all this is a proof of correctness our method and purpose. So far, no research has been done to treat diabetes through CRISPR technology. According to the research of Frederick and his colleagues, the lack of mir-200c prevents the apoptosis of beta cells to some extent, so by knocking out mir-200c, we will reach the same result as they did.

Keywords: CRISPR, diabetes, beta cells, SnapGene

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Detection of Acinetobacter baumannii strains isolated from Intensive Care Units (ICU) (Research Paper)

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Introduction: Recently, A. baumannii appears significantly in the form of endemic and epidemic in hospitals. In the clinical setting, A. baumannii is extremely dangerous, due to it is the ability to colonize and infect severely immunocompromised patients in ICUs. The aim of this study was to determine the Detection of Acinetobacter baumannii strains isolated from the Intensive Care Units (ICU) of Isfahan

Methods: During one one-year period (2021-2022), 200 samples of Suspected Acinetobacter baumannii were assembled from the ICUs of Isfahan hospitals. A. baumannii was confirmed by conventional phenotypic and biochemical experiments. For definitive diagnosis A. baumannii PCR assay was performed for OXA_51-like gene. The susceptibility of isolates was determined by the standard disk diffusion technique according to CLSI

Results: In this study, 100 isolates were Confirmed as A. baumannii. The antimicrobial patterns of isolates showed that 95% to imipenem, 90%Cefepime, and meropenem, 85% to trimethoprim-sulfamethoxazole, 80% to Ceftazidime, 70% to Tetracycline, 40% of isolates were resistant to Amikacin. All isolates were resistant to Ciprofloxacin

Conclusion: In this study A. baumannii, was high in resistance to antimicrobial agents. Strategies to control these strains in the treatment center should be implemented.

Keywords: Acinetobacter baumannii.Intensive Care Units. Antimicrobial agents

Detection of virulence Genes of Escherichia coli O157:H7 strains from Urinary tract infections in Isfahan (Research Paper)

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Introduction: E. coli O157:H7 is one of the main factors that lead to diseases such as diarrhea, bleeding colitis, uremic hemolytic syndrome, and even death in men. This study aimed to determine and survey the prevalence of Escherichia coli O157:H7 virulence Genes from Urinary tract infections in Isfahan

Methods: In this study 100 urine samples were collected from nosocomial infection during 6 months. Then, isolates were identified with specific tests. Then isolation of E.coli O157:H7 was confirmed with the use of specific antisera and the presence of E.coli O157:H7 virulence genes including stx1, stx2, eaeA was analyzed with multiplex PCR method

Results: From50 strains of E.coli O157:H7 isolated,20 % of the isolates with genes stx2 and eaeA. the stx1 gene was in 10 % of the isolate. and no isolates were observed with all three genes.

Conclusion: E.coli O157:H7 strain is an important public health concern. Preventive measures may reduce the number of who carry it.

Keywords: E.coli , urinary tract infections, multiplex PCR

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Detection of PDK1 gene expression difference and clinicopathology of samples in paraffin block tissues of gastric adenocarcinoma (Research Paper)

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Introduction: Gastric cancer (GC) is a multifactorial disease, where many factors can influence its development, both environmental and genetic. Current statistics display GC as the fourth leading cause of cancer deaths worldwide, where the rate of median survival is less than 12 months for the advanced stage. Gastric carcinoma as a malignancy of a high aggressiveness with its heterogenous nature, and still constitutes a global health problem. That is why alternative prevention, considered as a proper diet, early diagnosis and follow-up proper treatments, leads to the reduction of recorded incidents. In this research, we will investigate the difference in the expression of PDK1 gene in the tissues of healthy people or tumors with stomach cancer in order to determine the diagnostic value of PDK1.

Methods: In this study, after collecting samples, RNA extraction and cDNA synthesis were performed. Then, we used the Real-time PCR technique to check the gene expression, and the data obtained from it were analyzed through Rest2009 software.

Results: Finally, after analyzing the data obtained from the Real Time PCR reaction, it was found that the PDK1 gene had a significant difference in expression between healthy and tumor tissue, so that its increased expression in tumor tissue was confirmed.

Conclusion: The significant expression difference of PDK1 and the obtained data show that this gene can be introduced as a gastric cancer biomarker. More research should be done to be sure.

Keywords: Gastric Cancer , PDK1 , Real Time PCR

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Detection of PI3K gene expression difference and clinicopathology of samples in paraffin block tissues of gastric adenocarcinoma (Research Paper)

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Introduction: Gastric cancer is a global health problem, with more than 1 million people newly diagnosed with gastric cancer worldwide each year. Despite its worldwide decline in incidence and mortality over the past 5 decades, gastric cancer remains the third leading cause of cancer-related death. Knowledge of global as well as regional epidemiology and risk factors for gastric cancer is essential for the practicing gastroenterologist to make personalized decisions about risk stratification, screening, and prevention. In this article, we will examine the expression of PI3K gene and it`s regulators and compare this expression difference between tumor and healthy tissue.

Methods: In this study, after collecting samples, RNA extraction and cDNA synthesis were performed. Then, we used the Real-time PCR technique to check the gene expression, and the data obtained from it were analyzed through Rest2009 software.

Results: The results of the data analysis showed that the expression of PI3K gene increased in tumor tissues compared to healthy ones, and this expression difference between healthy and tumor tissue is significant.

Conclusion: The significant expression difference of PI3K and the obtained data show that this gene can be introduced as a gastric cancer biomarker. More research should be done to be sure.

Keywords: Gastric Cancer , P13K , Real Time PCR

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Detection of RICTOR gene expression difference and clinicopathology of samples in paraffin block tissues of gastric adenocarcinoma (Research Paper)

Dr.Faranak Jamshidian,[1,*] De.ShohreZare,[2]

1.
2.

Introduction: Background : Cancer has affected a lot of people and it is the second leading cause of death in the world after heart diseases for many years .And it is vascular. Cancer is a very complex genetic, epigenetic, and environmental disease with great diversity in tissue, tumor, and cellular levels. Scientists are trying to propose the best option for each patient's treatment regimen by accurately identifying the mutations involved in the development of each cancer, in order to prevent the side effects of chemotherapy as much as possible with this approach and to maximize the efficiency of the treatment RICTOR overexpression was associated with increase of tumor size, lymph node metastasis, and advanced TNM stage with poorer overall survival. RICTOR attenuates cell cycle progression and increases of apoptosis. Previous research has identified RICTOR as an important mediator of tumor progression and metastasis. identified that mTOR is a serine-threonine protein kinase that belongs to the family of phosphoinositide kinase-3 (PI3K) related kinases and plays an essential role in cell metabolism, growth and survival. Based on its sensitivity to rapamycin, mTOR was classified into two structurally and functionally distinct multiprotein complexes called mTOR complex1(mTOR1) and mTOR complex2(mTOR2) Extensive research has shown that mTORC plays an important role in the PI3K-AKT pathway, promoting cell metabolism, growth, and survival. RICTOR is a component of the mTORC2 complex that determines the stability and integrity of the mTORC2 complex. Many studies have shown that mTOR overexpression is common in gastric cancer, and p-mTOR is suggested as an independent prognostic factor for gastric cancer. As early as 1984 , the first generation of mTOR inhibitors, rapamycin, was used for tumor treatment subsequent reports showed that the combination of rapamycin and other anti-tumor drugs had a very good effect.

Methods: First, gastric cancer tissue samples were collected from patients by a specialist doctor, and then RNA is extracted from the tissue. After collecting samples, RNA extraction and cDNA synthesis we effectuate. All work steps are done under the laminar hood.

Results: After some researches, there was a significant increase of the expression of Rictor gene in cancer samples compared to the samples of healthy people.

Conclusion: Considering that the effect of this gene on gastric cancer has increased, it can act as a biomarker for the prevention of gastric cancer.

Keywords: Gastric cancer,RICTOR gene, Clinicopathology

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Detection of the Common MicroRNAs Associated with Breast Brain Metastasis: A Bioinformatics Survey (Research Paper)

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Introduction: Breast brain metastasis rates is in a rise due to higher survival rates of the patients. It is necessary to obtain more detailed information on the impacts of deregulations in the expression of microRNAs (miRs) and mRNAs with regard to the etiology of breast brain metastasis since a metastatic process necessitates a complicated setting such as a suitable niche.

Methods: Aiming to detect the important molecular pathways and important miRs in the breast brain metastasis, we searched for publically available microarray studies on this subject from the Gene Expression Omnibus database (GEO) data base. Two miR data sets (GSE134108 and GSE37407) as well as one mRNA data set (GSE52604) were selected. GEO2R, an interactive web tool, was used to compare two group of samples in each GEO series in order to discover the differentially expressed miRs (DEMs) and the differentially expressed genes (DEGs). The list of common up regulated miRs was detected, then the list of target genes of theses common miRs that were also consistent with downexpressed DEGs, the important pathways and protein-protein interactions (PPI) were detected.

Results: The miRs data sets consisted of GSE134108 on the subject of brain metastasis-related miRs in the serum samples of patients with advanced breast cancer, and GSE37407 that was miR expression profiling from tissue samples and the gene expression profiling study with GSE52604 used tissue samples. In total, we detected 4 shared DEMs (hsa-miR-200a/b/c family and has-miR-141) and 131 common DEGs. The most enriched term for the DEGs included Focal Adhesion in pathway analysis, head development in biological processes analysis and a PPI network was provided as well.

Conclusion: In conclusion, members of miRs-200 family (miR-200a/b/c) as well as miR-141 potentiate advanced breast cancer patients for developing a metastasis of cancer cells into the brain tissue, and these miRs might represent biomarkers for this process.

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Keywords: Breast cancer, Brain Metastasis, Bioinformatics, microarray, microRNA

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Determination of Flavonoid Compounds with Antidiabetic Properties in Medicinal Plants and Fruits by HPLC (Research Paper)

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Introduction: Interest in the determination of the concentrations of flavonoid compounds, which have antidiabetic properties, in medicinal plants and fruits by HPLC has been increased in recent years. In particular, the widespread use of HPLC systems with good separation capability allows us the determination of concentrations of these compounds in more food samples. Diabetes mellitus is a metabolic abnormality with hyperglycemia. This disease is due to defects in the secretion or activity of insulin or both. Various researches have shown that flavonoids, as one of the important anti-diabetic substances in plants, are able to reduce blood sugar and increase secretion and sensitivity of insulin. The positive effect of flavonoids due to the Increasing the intracellular amount of vitamin C Preventing permeability and rupture of capillaries and strengthening the body's immune system, affects the pancreas and its beta cells and treats diabetes. On the other hand, the consumption of flavonoids that have hıgh antioxidants activity clean free radicals ın body. The aim of this study was to use the HPLC method to analyze Flavonoids such as quercetin, apigenin and catechin are found in medicinal and aromatic plants and fruits such as green tea (Camellia sinensis L.), dill (Anethum graveolens L.), sage (Salvia fruticosa MILLER.), chamomile (Matricaria chamomilla L.), and pomegranate (Punica granatum L.).

Methods: HPLC was used for the determination of these components. Optimal parameters for HPLC were determined before quantitative analysis. Parameters injection volume 20 microliter column temperature 35 oC and the flow rate was found 1 ml/min for all 3 compounds. Different parts of plant samples were used such as leaves of green tea, leaves and above ground parts of dill and sage tea, flowers of chamomile and peel of pomegranate. The samples are washed with pure water after collection Then these were dried and turned into powder. The dried samples were milled. Then 5 g of the samples were weighed and a solution was prepared by 25 ml of ethanol (80%-Water). The solutions were incubated with stirring at room temperature for 24 hours. thenThe extracts were filtered by Whatman filter paper 1.

Results: The analysis results show that, catechin concentration in green tea, dill and sage tea and, chamomile flower and pomegranate peel was respectively 24.2666, 6.8694, 6.8990, 4.7631, 11.2824mg/ml. Quercetin concentration was in sage tea and dill and pomegranate peel respectively was 3.0461, 1.7850, 0.7029 and it was not found quercetin in green tea leaves and chamomile flowers. Apigenin concentration was in chamomile flowers and sage tea, respectively, 3.5599, 2.9129 and not found in others. Total quercetin, apigenin and catechin concentrations in selected samples were detected in green tea, dill and sage chamomile flowers and pomegranate peel, respectively. 24.2668, 8.6544, 12.8580, 8.3230 and 11.9853 mg/ml.

Conclusion: The analysis results show that the highest and lowest quercetin concentrations were respectively: Sage (Salvia fruticosa MILLER.), 3.0461mg/ml and pomegranate peel (Punica granatum L.) 0.7029 mg/ml, were found. The highest and lowest apigenin concentrations were found in chamomile (3.5599mg/ml) and sage (2.9129mg/ml) It was observed that the highest catechin concentration was found in green tea (24.2668) and pomegranate peel (11.2824) and the lowest 6.8694mg/ml catechin concentration was found in dill (6.8694mg/ml). In the samples we selected, the highest total quercetin, apigenin and catechin concentrations were 24. 2668mg/ml in green tea and lowest concentrations were found 8.3230 mg/ml in chamomile. The results of our study on the use of the extracts of the plants we used for this purpose are qualified and may lead to the candidate for new products that can be used in the regenerative treatment of diabetic patients. In future studies, catechin, quercetin and apigenin may be isolated from these plants and added to foods to help balance blood sugar. The data obtained as a result of this analyzes may lead to the development t of new antidiabetic drugs and will enable scientific evaluation of the effectiveness of these plants, which are used as antidiabetics among the public. These plants can be a source for herbal medicines. Thus, natural drugs with reduced side effects can be obtained.

Keywords: Diabetes Mellitus, Flavonoid, HPLC, Medicinal Plants

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Determining the effect of nanocurcumin loaded on nanofiber scaffolds on osteoporosis fracture repair in adult ovariectomized Wistar rats (Research Paper)

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Introduction: The present study was conducted to investigate the effect of nanocurcumin loaded on nanofiber scaffolds on the fracture healing process caused by osteoporosis in ovariectomized adult Wistar rats.

Methods: 32 three-month-old adult wistar rats weighing 220 to 250 grams were ovariectomized. After 3.5 months, the OP progression was evaluated using CT scanning and the critical size defect was made on the femur bone. Then, the rats were divided into the following groups: 1) ovariectomy + fracture group, 2) ovariectomy + fracture + scaffold group, and 3) Ovariectomy + fracture + scaffold containing nanocurcumin group. At four and eight weeks after surgery, western blot analyses were performed to evaluate OPG, OCN, and Runx2 proteins in local fractures.

Results: After 4 weeks, the expression level of osteoprotegerin in groups 2 and 3 was significantly higher than group 1 ($p<0.001$) and the expression level of osteocalcin was significantly higher in group 3 than group 1 ($p<0.05$) but there was no significant difference between groups 1 and 2 in terms of osteocalcin expression. The expression level of collagen type 1 in group 3 was significantly higher than group 1 ($p<0.0001$) and also in group 2 was significantly higher than group 1 ($p<0.01$). After 8 weeks, the level of osteoprotegerin expression in groups 2 and 3 was significantly higher than group 1 ($p<0.001$) and the level of osteocalcin expression was significantly higher in group 3 than group 1 ($p<0.0001$). There was no significant difference between groups 1 and 2 in terms of osteocalcin expression. Also, there was no significant difference in collagen type 1 expression and RUNX2 expression between group 3 vs. 1 and group 2 vs. 1.

Conclusion: The results of this study showed that the use of scaffolds containing nanocurcumin can help in the repair of fractures caused by osteoporosis.

Keywords: Nanocurcumin, Scaffold, Osteoporosis, Fracture, Ovariectomy

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Determining the inhibitory dose of Actinomycete bacteria extract on the osteogenic potential of adipose mesenchymal stem cells (Research Paper)

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4.

Introduction: Aim and background: Actinomycete bacteria (Ac) is a suitable source for the production of anti-bacteria, anti-cancer and anti-inflammatory agents. Adipose tissue mesenchymal stem cells (ADMSCs) are multipotent stem cells that have the ability to regenerate bone damages. In the current study, we aimed to determine inhibitory dose of a new Ac extract on the osteogenic potential of rat ADMSCs.

Methods: Materials and Method: Ac was collected from Garmsar region of Iran and cultivated in 25 pages in the basic culture medium and extracted using ethyl acetate solvent. ADMSCs were isolated from fat tissue of Wistar rats and cultured in DMEM-F12 medium supplemented by 10 % FBS and 1% antibiotics. For osteogenic differentiation, ADMSCs were cultured in the presence of induction factors and Ac extract applied to cells at a concentration of 10 and 20 µg/ml for 21 days. Alizarin red staining and alkaline phosphatase assay were used to measure osteogenic differentiation.

Results: Results: The results of alizarin red staining and ALP assay revealed that Ac had inhibitory effect of osteogenic differentiation of ADMSCs at concentration of 20 µg/ml ($p > 0.05$) in compare to 10 µg/ml.

Conclusion: Conclusion: The findings of this study showed that Ac had a dose-dependent effect on the osteogenic potential of ADMSCs that should be considered in its applications.

Keywords: Keywords: Actinomycetes, Adipose Mesenchymal stem cells, Bone, Osteogenesis

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Determining the resistance pattern of Shigella bacteria to antibiotics in different populations (Research Paper)

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Introduction: Shigellosis is the most common in developing countries and this disease is the second cause of death in children under 5 years of age (11%). on of the common causes of this disease is malnutrition, and the problems that arise as a result of this disease are low physical and mental growth. due to the resistance of shigella bacteria to antibiotics, Shigellosis is very worrying as an inflammatory diarrhea agent in Iran therefore, the aim of this study is to investigate the pattern of antibiotic resistance in Tehran

Methods: First, we use MAC and XLD agar, then take created colony to the gallery tests to determine the serotypes of shigella bacteria, we perform a serological test, and if the agglutination results is positive mass is formed. and finally, it is Time to perform an antibiogram test to detect the sensitivity of shigella bacteria strains to antibiotics

Results: the shigella strains were isolated from 36 patients with bloody diarrhea (10%). overall, 36% isolates were positive for shigella spp. of which 16 (44.44%) serotypes were identified as shigella flexeneri, 10 (27.77%) serotypes were identified as Shigella sonnei, 2 (5.55%) serotypes were identified as Shigella boydii and 8 (22.22%) serotypes were identified as Shigella dysenteriae. shigella flexeneri is the most common and antibiotic susceptibility test revealed that the lowest resistance percentage was related to ciprofloxacin and Cefixime that were the best antibiotics against Shigella isolates

Conclusion: we concluded that strains shigella bacteria from contaminated fecal-oral route and contaminated water and food be transferred. and this is one of the causes of diarrhea in Tehra. since the drug resistance pattern of Shigella differs geographically and over time within a country, continuous and regular surveillance program is necessary

Keywords: shigella bacteria, Shigellosis, antibiotic resistance, Tehran, shigella strains

Developing a CRISPR/Cas9 plasmid vector containing specific single guide RNAs targeting sonic hedgehog signaling pathway: an anti-cancer approach (Research Paper)

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Introduction: Clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) system is an effective genomic engineering tool applied in gene/cancer therapy. This study aims to develop a vector for efficient targeting of sonic hedgehog (SHH) signaling pathway.

Methods: For developing the SHH-targeting plasmid vector, a gRNA (guide RNA) cassette containing three efficient and specific gRNAs was designed by CRISPOR online platform and synthesized. Then it was cloned into the Cas9 expressing plasmid vector, pCas-guide-EF1a-GFP, following digestion by BamHI and BsrGI restriction enzymes, and ligation with T4 ligase. Then the ligation mixture was chemically transformed and proliferated in competent E.coli DH5α. Following plasmid extraction, the polymerase chain reaction (PCR), and DNA sequencing was performed to confirm the presence of gRNA cassette.

Results: Three specific, and efficient gRNAs for second, fourth, and sixth exons of SMO gene were carefully selected and successfully synthesized. Cloning of the gRNA cassette into the pCas-guide-EF1a-GFP vector was confirmed by PCR, and sequencing of the gRNA cassette.

Conclusion: Developing specific, and efficient CRISPR/Cas9 vectors to target positive regulators of neoplastic pathways is a promising approach in anti-cancer target therapy which may lead to better understanding of various

molecular pathways leading to cancer, and developing meticulous chemotherapy agents.

Keywords: CRISPR/Cas9, plasmid, vector, SHH, cancer

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Development of e-learning and its contribution to continuing medical education of healthcare professionals (Review)

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Introduction: In recent years, the outbreak of the COVID-19 pandemic has affected the education system in addition to the health system (HS). Since the beginning of this pandemic, educational systems around the world have been widely conducting their education in the form of e-learning and until today, this new method has replaced the previous methods. The increasing use of e-learning obliges the educational policy makers (EPMs) of the HS to benefit from this new method. Considering the importance of the role of continuous education and updating information in improving the quality of health care, this study was conducted with the aim of investigating the impact of e-learning in the continuing medical education (CME) of healthcare professionals (HCPs).

Methods: In this systematic review, publications were retrieved by using keywords and searching in valid bibliographic database, including Medline, EMBASE, Scopus, Web of Science, Google Scholar, PubMed and ScienceDirect. The language of search was restricted to English. The statistical population of this study includes all articles published until 2023. Finally, after evaluating the data quality, we analyzed a total of 21 articles.

Results: The findings from the study of the articles showed that the most important reason for the significant growth of the use of e-learning in the CME can be considered to be cost-effectiveness (CE). We found that reducing the cost of conducting continuous education courses, the possibility of flexible planning, reducing travel time for face-to-face training, and reducing the cost of accommodation can be counted as the main reasons for being CE. Providing the opportunity for non-attendance training and not limiting the number of participants in many courses has led to the appropriate reception of e-learning for CME, but the effectiveness and success of this method has been dependent on long-term use by HCPs. Compensating for the lack of training instructors for HCPs, quick transfer of knowledge and easy access to resources are also important achievements of e-learning in low- and middle-income countries. Also, the review of the articles of this research showed that the effect of factors such as age, race, nationality, ethnicity and gender on the effect of e-learning of HCPs has been neglected.

Conclusion: The results of this research show that the development of e-learning from the beginning of the COVID-19 pandemic until today has greatly helped in achieving the goals of CME. Based on the findings of this research, the EPMs of the HS have emphasized the use of e-learning as much as possible and consider it an effective method to improve the learning of HCPs and provide better health care. Considering the development of e-learning and its increasing use in the field of medical education, future researches will certainly increase its effectiveness by considering other factors that can be investigated.

Keywords: E-learning, continuing medical education, healthcare professionals

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Development of nanofibers in antibiotic delivery to combat methicillin-resistant Staphylococcus aureus (Review)

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Introduction: Infectious diseases are one of the major causes of mortality rates in the world. The onset of methicillin-resistant Staphylococcus aureus (MRSA) has become a global concern in public health due to antibiotic resistance. The use of drug delivery systems is an effective way to rise drug stability and decrease antibiotic use. Nanofibers are versatile materials with numerous applications, from drug delivery to antibacterial carriers

Methods: Electrospinning is a versatile method to make micro- nano fibers by ejecting polymer solutions through a syring which could be coaxial or simple , under a high voltage.

Results: In this review, we focus on emphasizing challenges in treatments and drug delivery, especially antibiotics with nanofibers. Additionally, we provide an overview of current studies into the development of improved Methicin delivery systems using electrospun nanofibrous membranes for biomedical and tissue engineering applications.

Conclusion: There are different types of nanofibers based on the method of preparation, such as core-shell, hollow, porous, and non-porous nanofibers. One of the main applications of nanofibers is using them as carriers for the delivery and release of antibiotics in a particular time and space.

Keywords: Methicillin-resistant Staphylococcus aureus Advanced drug delivery Drug resistance Nanofibres

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Diabetic Foot Ulcers(DFU)review articles (Review)

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Introduction: Diabetes, a disease related to lifestyle, is characterized by chronic hyperglycemia and imposes serious problems. The prevalence of diabetes is rapidly increasing worldwide and a real epidemic of the disease is expected in this century. Egypt is ranked the eighth country worldwide in the number of diabetic patients, and by 2045 it is expected to be the sixth country. Diabetes is a systemic disease that affects almost every part of the body, and the feet are frequently the first to suffer. The proportion of male patients was greater than females, and it was noted that the age group (51-68 years) was more affected by diabetic foot. Diabetic foot infection (DU) was considered to be one of the most common and dangerous diabetes complications. So, the most common cause of hospitalization and non-traumatic lower limb amputation is diabetic foot ulcer. It could lead from soft tissue infection to bone infection and is a leading cause of lower limb amputation. DFU patients have a 2.5 times higher risk of death compared to diabetic patients without foot ulcers. Diabetic foot ulcers, fi left untreated, can become infected and cause other complications, such as gangrene, osteomyelitis, and amputation. Surgery and antibiotic therapy are the options used to control this infection.

Methods: In patients with a healed DFU, significant independent risk factors for DFU recurrence during a 3-year follow-up period, despite intensive foot care, were: plantar ulcer location, presence of osteomyelitis, HbA1c>7.5%, and C-reactive protein (CRP>5mg/I. The major predisposing factor to foot ulceration leading to infection is usually related to peripheral neuropathy. Mostly the diabetic foot infections are mixed bacterial infections and the proper management of these infections requires appropriate antibiotic selection based on culture and antimicrobial susceptibility. The presence of drug-resistant bacteria in diabetic foot ulcers creates a big challenge during the treatment, so nanotechnology has been applied to find an alternative solution instead of antibiotics. Silver metal has been used in medicine since around 4000 B.C, even before it was recognized that bacteria constitute the primary cause of infection. The aim of this study, is comparing the antibacterial activity of silver nitrate and silver nanoparticles, finding that AgNPs had a high antibacterial effect against isolated bacteria more than AgNO3, primarily due to their nano-size.

Results: aureus (26%) was the most common bacteria isolated, followed by E. coli (20%) and Enterococcus spp (15 percent). Extended- spectrumbeta-lactamase (ESBL) producers made up 53% of the Gram-negative bacteria, Methicillin -resistant staphylococcus aureus (MRSA) made up 41%, and Vancomycin- resistant enterococci (VRE). made up 19%. Herbal products through different mechanisms of action, including antimicrobial, anti-inflammatory, antioxidant activity, stimulation of angiogenesis, production of cytokines and growth factors, keratinocytes, and fibroblast migration and proliferation may be considered as an important support during conventional therapy or even as a substitute for synthetic drugs used for diabetic wound treatment.

Conclusion: aureus is the most common cause of diabetic foot ulcers. Due to Staphylococcal surface proteins such a s (protein A) assist the bacteria to cling to the skin and facilitate the bacterial colonization in the diabetic foot, and then release many of the virulence factors that invade the immune system such as 3-hemolysin.

Keywords: DFU, staphylococcus aureus, Infection, Diabetic Foot Infection, Diabetic Foot Ulcers, Hyperglycemia

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Diagnosis of the exon 47 deletion in the DMD gene by isothermal amplification method (Research Paper)

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Introduction: Duchenne Muscular Dystrophy (DMD) is one of the most prevalent neuro-genetic disorders in Iran. DMD is an X-linked recessive disorder characterized by severe, progressive, and muscle-wasting symptoms. The onset of DMD symptoms is between 2-5 years and consists of hypertrophy in the calf muscles, waddling walk, trouble climbing stairs, walking on toes, repeated falls, Gower's sign, and progression of muscular degeneration. The Dystrophin gene is the largest known gene in human genomes and consists of 79 exons. The main cause of this disorder is deletion (66%), then duplication (7.5%). Deletions are more common in the two hotspot regions of the DMD gene which include exons 1–22 and exons 43–55. Based on vast and recent research in Iran, the most frequent deletions occur in exons 50 (6.8%), 48 (6.4%), 46 (6.2%), 49 (6.2%), 47 (6.0%), 51 (6.0%) and 45 (6.0%) respectively. Multiplex-PCR and MLPA are the most common tests in order to identify the deletions. Using isothermal techniques for the detection of the mutations could be a point of care and alternative approaches for the diagnosis of the disease. The aim of the present study was to identify the exon 47 deletion of the DMD gene using Gap-LAMP (Loop-mediated isothermal amplification) method.

Methods: The DNA sample of one patient that has exon 47 deletion in the DMD gene was collected from Kariminejad-Najmabadi Pathology & Genetics Center. The genomic DNA of the healthy individuals was extracted using the phenol-chloroform DNA extraction method. We designed 6 primers for detecting exon 47 of the DMD gene and 6 primers for the Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) Gene as internal control by LAMP primer designing software PrimerExplorer-5 (https://primerexplorer.jp/e/). The LAMP reaction was performed on a total of 20µl containing Bst-2 DNA Polymerase manufactured by New England Biolabs. The reaction mix was incubated for 30 minutes at 65° centigrade. The agarose gel electrophoresis was applied for the Visualization of the LAMP products.

Results: The results of the study showed that the designed method could amplify the target region of the control group while this region was not

detected in the patients due to the deletions. The GAPDH region was successfully detected in all Samples.

Conclusion: LAMP is an isothermal nucleic acid amplification technique in which the reaction is carried out at a constant temperature, and does not require a thermal cycler. This method has usually been used for the identification of infectious agents. The present study showed that this method can be used for detection of deletions in human DMD genes. Since LAMP is performed in an isothermal condition that does not require a thermal cycler device it can be used as a screening method for the detection of the deletions in DMD patients. Further studies are recommended to design Gap-LAMP approaches for detection of deletions in all exons of DMD gene.

Keywords: Duchenne muscular dystrophy, Isothermal amplification, Diagnosis deletion mutation

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Diagnostic effect of CRISPR/Cas12 on JAK2 in lung cancer (Review)

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Introduction: Lung cancer constitutes the primary cause of cancer-related mortality. This malady encompasses subtypes such as small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Conventional diagnostic approaches may not be as effective as CRISPR/Cas12 in the diagnosis and modification of mutations. The latter technique is a highly accurate and efficient tool that can enable a more precise diagnosis of this disease. Notably, CRISPR/Cas12 can detect specific genomic sequences with exceptional precision. JAK2 encodes a non-receptor tyrosine kinase that plays a fundamental role in the development of lung cancer by regulating cellular growth and division. This gene undergoes mutation and decreased expression, and its signaling pathway is crucial in the formation of lung cancer.

Methods: By comparing lung biopsy tissue of patients and healthy people, researchers have found that the increased methylation of JAK2 during cancer development can be detected by CRISPR/CAS12a, thereby facilitating an early diagnosis of lung cancer. For instance, a CRISPR/CAS12a-based nucleic acid detection system that integrates PCR amplification with Cas12a-mediated cleavage can detect the V617F (a common mutation in JAK2), and through the fluorescent detection system in PCR, it can produce strong signals and diagnose the mutated DNA.

Results: In one study involving 14 samples (one patient and 13 healthy controls), CRISPR/Cas12a successfully identified the presence of mutated samples.

Conclusion: Recent studies have investigated the effect of JAK2 gene in the treatment of lung cancer, and we hope that CRISPR will gain approval and lead to the development of a definitive treatment for this disease.

Keywords: Lung Cancer / JAK2 / CRISPR

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Diagnostic of Cytokeratin-19 Gene Expression in Iranian Breast Cancer Patients (Research Paper)

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Introduction: Breast cancer is the most common malignancy and the leading cause of cancer-related mortality in women (1). Circulating tumor cells (CTCs) in the blood can be an important prognostic indicator for breast cancer patients (2). In both primary and metastatic breast cancer patients, tumor markers consist of various molecules that can be detected in plasma or other body fluids and tissues (3). A diagnostic tumor marker can be used to help in the diagnosis of a disease.CK19, one of the three main keratins besides CK8 and CK18 expressed in the simple and stratified epithelium and various carcinomas including breast cancer (9), is cleaved by caspase 3, and the soluble fragments are released and detected in cancer patients

Methods: General information Breast cancer specimens from 50 women (mean age of 40.2 ± 65.55 years) who had undergone surgery at the Tehran University-affiliated hospital and Shohadaye Tajrishbased referral and teaching hospital affiliated to Shahid Beheshti University of Medical Sciences were collected. Also, normal breast tissues (N = 50) were taken from the same patients that had undergone partial or total mastectomy. Data for all patients were collected for analysis. All of them were diagnosed with breast cancer without metastasis and tested by IHC staining. Patients were assigned on the basis of national/international breast cancer protocols and the study was approved, according to local law and regulations, by the Institutional Review Boards of each participating referral hospital. Written informed

consent was requested from patients and a questionnaire have been administered

Results: The expression level of CK19 from tumor tissues increased significantly (P=0.21) compared to controls. Also, the expression level of metastatic lymph nodes increased significantly.

Conclusion: While additional validation studies are needed, the present investigation showed that CK19 can be detected in peripheral blood samples of breast cancer patients, and can predict SLN status before surgery. Further, the CK19 copy number was strongly correlated with the number of metastasis-positive LNs.

Keywords: Gene expression, quantitative PCR, Metastasis, Sentinel lymph node

Differentially Expressed Wound Healing-Related Transcriptome in the Non-Healing Diabetic Ulcers (Research Paper)

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Introduction: Cutaneous wound healing is a complex process and composed of sequential cascade events in which chronically unhealed wounds/ulcers cannot complete individual phases or the entire healing process. It should be noted that peripheral arterial disease (PAD) is the most common cause of non-healing ulcers, especially indiabetic patients. In fact, several factors can cause chronic wounds not to heal, but there is no doubt that diabetes plays a detrimental role in wound healing. Diabetic wounds are often characterized by excessive inflammation, decreased angiogenesis, wound hypoxia, and inadequate tissue perfusion. Dysregulated immune responses and impaired immune cell activation, proliferation, and survival also contribute to the pathogenesis of diabetic foot ulcers. The purpose of the research is to explore novel therapeutic target to overcome non-healing diabetic wounds.

Methods: miRNA data sets were achieved by searching in GEO database until September 2023. The studies containing high throughput miRNA dataset and work on both healthy and diabetic patients were selected for further analysis. To identify differentially expressed genes (DEGs), eligible gene expression profiles were investigated using the GO2R package, |LogFc|>1, and adj.P.value<0.05. To create and analyze the protein-protein interaction networks, STRING (12.0) and Cytoscape software (Cytohubba and MCODE plugin) were applied. The miRSystem server was used. MiRNA target interactions were also determined using Mirwalk and miRTarBase. Finally, the DAVID database was used for finding significant molecular pathway, gene ontology, and enrichment analysis.

Results: According to the DEGs identified from 4 eligible datasets, miR-122 which has an effective role in inflammatory pathways such as mTOR, PI3K, and NF-kB as well as metabolic pathways, is a significant common miRs in

both diabetics and diabetic + PAD patients. The key and hub genes in diabetic wounds compared with healthy wounds were CCL2, CXCL8, MMP9, and HBS1, which are involved in inflammatory processes, neutrophil chemotaxis, innate immune cell responses, angiogenesis, binding to collagen, integrin, and extracellular matrix supporting that these genes are promising candidates to prevent non-healing wound in the patients who suffers from diabetes. The target miRNAs for them via miRTarBase include hsa_miR_124_3p, hsa_miR_495_3p, and hsa_miR_183_5p.

Conclusion: Our findings confirmed that miR-122 contributes to the development of non-healing wounds especially in inflammatory process which is the first step of wound healing. Moreover, our study offers new potential targets to improve wound healing in patient with diabetic and diabetic + PAD.

Keywords: diabetes, non-healing ulcers, chronic wounds, GEO datasets

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Dissociative Identity Disorder: Clinical Implications and Treatment Options (Review)

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Introduction: Dissociative Identity Disorder (DID) is a complex psychiatric condition characterized by the presence of two or more distinct identities or personality states within an individual. This disorder poses significant challenges for both clinicians and patients due to its intricate symptomatology and the potential impact on daily functioning. Understanding the clinical implications and treatment options for DID is crucial for providing effective care to affected individuals. In this study, we will explore the current diagnostic criteria, incidence and prevalence rates, causes, symptoms, impacts, and treatment approaches for DID.

Methods: To gather relevant information for this paper, an extensive literature review was conducted using various academic databases such as PubMed, PsycINFO, and Google Scholar. Keywords such as "dissociative identity disorder," "clinical implications," and "treatment options" were utilized to identify relevant articles, case studies, and research papers. Only peer-reviewed sources published within the last 10 years were considered for inclusion.

Results: The current diagnostic criteria for DID are outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). According to the DSM-5, the essential features of DID include the presence of two or more distinct identities or personality states, recurrent gaps in the recall of everyday events, and significant distress or impairment in functioning. The disorder is relatively rare, with an estimated prevalence rate of approximately 1-1.5% in the general population. The exact causes of DID are still not fully understood. However, it is believed to develop as a response to severe childhood trauma, particularly instances of repetitive physical, sexual, or emotional abuse. The fragmentation of identity is thought to be a coping mechanism that allows individuals to escape from overwhelming or traumatic experiences. Symptoms of DID can vary widely among individuals, but common features include amnesia, depersonalization, derealization, identity confusion, and identity alteration. These symptoms can significantly impact an individual's daily life, relationships, and overall well-being. Treatment for DID involves a multimodal approach that typically includes psychotherapy, pharmacotherapy, and

supportive interventions. Psychotherapy, specifically long-term psychotherapy and specialized therapies such as cognitive-behavioral therapy for trauma-related disorders, has shown promising results in helping individuals with DID integrate their identities and develop healthier coping mechanisms.

Conclusion: Dissociative Identity Disorder presents complex clinical implications due to its unique symptomatology and impact on individuals' lives. It is crucial for healthcare professionals to be familiar with the current diagnostic criteria, incidence rates, causes, symptoms, and impacts of DID to provide accurate assessments and appropriate treatment interventions. The multimodal treatment approach, involving psychotherapy, pharmacotherapy, and supportive interventions, has shown promising outcomes in improving the quality of life for individuals with DID. Further research and understanding of this disorder are necessary to enhance clinical practices and improve treatment outcomes.

Keywords: Dissociative Identity disorder, DID, Cognitive-behavioral therapy, Trauma

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DNA methylation as a biomarker for the identification of liver cancer (Review)

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Introduction: Hepatocellular carcinoma (HCC) is a malignant cancer with high prevalence worldwide. The pathogenesis and progress of HCC is closely related to the unusual epigenetic regulation of hepatocytes. DNA methylation is a regulatory mechanism that is important in epigenetic studies and has been the subject of much research. In our review, the association of DNA methylation with the development and progression of liver cancer was investigated.

Methods: Reliable scientific sites and sources such as Scopus, Google Scholar, and PubMed were used to conduct this study.

Results: Investigation and study of traditional clinical factors and DNA methylation profile can be important in detecting neoplastic transformation at early stages in HCC-risk populations. As a result, CpG methylation can have an important application in the prognosis of HCC. Using DNA methylation profiles, clinical prediction can be provided in pre-treatment patient biopsies or plasma DNA.

Conclusion: Epigenetic changes and profiles such as DNA methylation can be related to biological characteristics of cancers and clinical symptoms of HCC patients. DNA methylation profiles can be used as surrogate biomarkers in clinical cancer studies.

Keywords: Hepatocellular carcinoma (HCC), DNA methylation, epigenetics

DNA methylation controls learning and memory (Review)

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Introduction: Learning and memory are two of the fundamental cognitive functions that confer us the ability to accumulate knowledge from our experiences. Although we use these two mental skills continuously, understanding the molecular basis of learning and memory is very challenging. Methylation modification of DNA is an epigenetic mechanism which is the most important process of neurons. DNA methylation regulates neural activities and memory formation via the control of gene expression in neurons, and relate these studies to various age-related neurological disorders that affect cognitive functions.And many types of human neurological disorders, including mental retardation (like MR) syndromes and neurodegenerative diseases, display cognitive defects as reflected by impaired learning and memory abilities , many other diseases with complex profiles, the underlying causes of most neural diseases are often heterogeneous and involve the interplays among different genes and environmental factors.

Methods: The function and behavior of neurons, like any other types of cells, are ultimately determined by the genes expressed in them. Synaptic connectivity among neurons serves as the physical basis for memory formation, which often entails gene products (mRNA or protein) from a vast number of neural activity-related genes. The molecular basis of synapse-dependent LTM formation can thus be understood by studying the regulatory mechanisms of gene expression in the neural network. DNA methylation and histone modifications regulate gene expression via reversible and dynamic chromatin remodeling processes. DNA methylation and histone acetylation can regulate gene expression synergistically through protein mediators such as the methyl-CpG binding protein MeCP2.also DNA methylation modification of the genome occurs primarily on cytosines located in CpG dinucleotides, posttranslational modifications of histone proteins are much more complex and affect multiple residues at over 30 sites within the N-terminal tails of histones. Histone methylation alone can appear in the form of mono-, di-, and tri-methylation. Even more complex, these different forms of methylation can occur on different amino acid residues that are located at different positions.

Results: Folate is an important substrate in one-carbon metabolism . Folate provides the dietary source of methyl group for biological methylation. It is

required for the conversion of homocysteine to methionine and the formation of S-adenosylmethionine . S-adenosylmethionine participates in biological methylation reactions, which generates S-adenosylhomocysteine that subsequently forms homocysteine. Folate-depletion can cause genomic DNA hypomethylation, which can be reversed upon dietary folate restoration. Folate depletion can also lead to cellular accumulation of S-adenosylmethionine and dramatically increase blood homocysteine levels. S-adenosylmethionine is a potent inhibitor of Dnmt activity through the product inhibition pathway and can lead to genome hypomethylation. The disruption of homocysteine metabolism can adversely affect both the developing and the adult brain. The disruption of one-carbon metabolism can repress the proliferation of cultured multipotent neuroepithelial progenitor cells and alter cell cycle distribution. And also folic acid deficiency dramatically reduces the number of proliferating cells in the dentate gyrus of the hippocampus in adults.Since neurogenesis in the adult hippocampus is possibly pivotal in learning and memory and in recovery from injury, these results suggest that dietary folate deficiency can affect neurogenesis via inhibiting the proliferation of neuronal progenitor cells in the adult brain

Conclusion: DNA methylation controls learning and memory

Keywords: DNA methylation - Folate - Histone methylation- Memory- Learning - Hippocampus

Does the Microbiota Affect Sleep or Is Sleep Affected by the Microbiota? A narrative review (Review)

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Introduction: Microbiota play an important role indubitable. The microorganisms that naturally inhabit the gut establish a symbiotic relationship with the host. Microbiota not only affects digestion of food but also in many researches are known as a crucial factor that plays a role bi-directionally in the metabolic, immune, and neural systems of the host, modulating the physiological and pathological function of many other organs and pathological function of other organs. In another hand, sleep also can influence multi factors like inflammation condition and loss of metabolic health as mentioned above. This study aims to investigate the role of gut microbiota as a factor in sleep disturbances.

Methods: The present review was conducted through the electrical scientific databases including PubMed, Scopus, and Scholar by searching with the keywords including "sleep", "gut-microbiota" and "microbiome" from 2014 to 2023 in English.

Results: The cross-sectional studies revealed similar findings regarding the relationship between sleep disturbance and gut microbial diversity. Among older adults, shorter sleep duration was linked to an increase in pro-inflammatory bacteria, while improved sleep quality was associated with a rise in beneficial Verrucomicrobia and Lentisphaerae phyla. However, in young adults, the impact of sleep disruption on the composition of the gut microbiome, particularly the ratio of beneficial Firmicutes to Bacteroidetes phyla, remains inconsistent and not fully understood. Some studies have shown that sleep deprivation in healthy individuals can change the gut microbiota even in a short period. The ratio of Firmicutes/Bacteroidetes is elevated, accompanied by an increased presence of Coriobacteriaceae and Erysipelotrichaceae families, while the Tenericutes families show a decrease. However, it should be noted that prolongation in the period of sleep deprivation can activate an adaptive response. Additionally, studies exploring the effect of chronic sleep fragmentation (SF) on gut microbiota support the hypothesis that sleep disturbance affects the gut microbiota, but the frequency of microbiota changes was reversed after 2 weeks compared to the initial changes. Transplantation of microbiota in mice yielded similar results,

indicating metabolic alterations as consequences of sleep problems. Besides the effect of sleep on gut microbiota, changes in gut microbiota or the use of prebiotics and probiotics can also affect sleep rhythm, such as an increase in non-REM sleep. Interestingly, in mice or individual that treated with antibiotics reported sleep emerge. Gaining a deeper understanding of this issue has the potential to offer novel therapeutic approaches for addressing various diseases. the cyclic nature of this relationship should not be neglected.

Conclusion: The relationship between gut microbiota and sleep is two-way. Previous studies suggest that low-quality of sleep and sleep disorder can change gut microbiota and also bacterial ratios in the gut can affect sleep quality. The possibility of utilizing treatments focused on restoring the gut microbiota holds promise in reducing the adverse effects of conditions like sleep apnea and mitigating their associated complications.

Keywords: sleep, gut-microbiota, microbiome, bacterial diversity

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Downregulation of LIPF affected by hsa-miR-2277-5p, FLG-AS1, and WDFY3-AS2 in a ceRNA network promotes the development of gastric cancer (Research Paper)

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Introduction: Gastric cancer (GC) is the fifth most common type of cancer in the world. Despite advances in medical treatment, GC is still a major cause of cancer-related deaths, ranking as the third most common cause of cancer death globally. Treatment for GC typically involves surgery to remove the tumor, followed by chemotherapy and/or radiation therapy to kill any remaining cancer cells, which is highly invasive. Therefore, finding a new biomarker can enhance monitoring and early detection. The theory of the competitive endogenous RNA (ceRNA) network suggests that long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) engage in a competitive regulatory mechanism that ultimately determines the induction or suppression of gene expression. In various cancer types, the interplay between the different constituents of this network undergoes alterations, thereby underscoring its potential utility as a biomarker for the diagnosis and treatment of cancer. The aim of this bioinformatics approach was to discover a set of genes, miRNAs, and LncRNAs that act in a biological network that remarkably impacts the progression of GC. As a potential biomarker in GC monitoring and early detection.

Methods: Raw data (GSE220917) was initially extracted from the NCBI Gene Expression Omnibus (GEO) for later analysis by Rstudio. The study included microarray raw data of RNA expression profiles of 23 samples (5 normal, 9 gastric cancer (GC), 9 gastroesophageal junction cancer), the 9 gastroesophageal junction cancer were later excluded and analysis was continued on GC and normal samples. Further analysis of raw data of microarray was conducted by Rstudio using “Limma” and “Affy” packages (downloaded from https://www.bioconductor.org) along with “pheatmap”, “dpylr”, “gplots”, and “ggplot2” packages (downloaded from https://cran.r-project.org) to find significant differentially expressed genes (DEGs). In this investigation, DEGs with adjusted p-value < 0.05 and |logFC| > 2 were considered significant. As a result of this analysis, LIPF was selected. Furthermore, GEPIA2 and ENCORI databases were used to validate the results of the analysis. In addition, biological pathway involvement was

processed through Reactome and NRICHR databases. Moreover, STRING was utilized to find significant protein-protein interactions among LIPF and other protein-coding genes. Finally, the possible interactions among LIPF with miRNAs and LncRNAs were verified by Mirwalk and miRNet respectively.

Results: Results of the microarray raw data analysis by Rstudio show LIPF gene is significantly downregulated in GC samples compared to normal samples (logFC = -7, adjusted p-value = 5.2 e-9). gastric lipase (LIPF) gene, which is connected with various lipid metabolism processes, is indicated to be significantly downregulated in this investigation. Therefore, the expression level of LIPF in GC seemed to be associated with local invasion, and disease stage. possible miRNA-mRNA interactions were determined using Mirwalk. As a result, six miRNAs were candidate to have significant interaction with the LIPF gene. These six candidates were later processed through the ENCORI database for further validations of mRNA-miRNA interaction and co-expression in GC progression. As a result, hsa-miR-2277-5p was selected to be negatively co-expressed with the LIPF gene. hsa-miR-2277-5p is shown to be overly expressed in GC samples and repress the activity of LIFP mRNAs. LncRNAs can act as miRNA sponges and have a regulatory effect on their target miRNAs. Therefore, selected miRNA was searched in miRNet to find interaction between them and lncRNAs in a ceRNA network. FLG¬-AS1 and WDFY3-AS2 were identified to have strong interactions with hsa-miR-2277-5p. FLG¬-AS1 and WDFY3-AS2 were later searched in ENCORI database to validate the miRNA-lncRNA correlation. Results of this study revealed that, all of these RNAs act as a ceRNA network that influences GC progression.

Conclusion: In conclusion, the downregulation of LIPF mRNA forms a possible ceRNA network along with hsa-miR-2277-5p, FLG-AS1, and WDFY3-AS2 Which proved to have a significant role in GC progression. With further investigation and experiments, this finding could be identified as a potential marker in GC early detection and monitoring.

Keywords: gastric cancer, ceRNA, bioinformatics

Downregulation of PCAT-1 long non-coding RNA in children with autism spectrum disorder (Research Paper)

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Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental childhood-onset disorder that can continue life-long. This disorder affects socio-communicative development and also causes rigidity and ritualistic/repetitive patterns of behavior. The prevalence of ASD is approximately 1 percent with a ratio of 4:1 in male to female. The etiological architecture of ASD is complex. Genetic and epigenetic factors play a crucial role in the pathogenesis of ASD and it has been estimated that up to 1000 genetic loci are potentially implicated in ASD. One of the factors involved in ASD is long noncoding RNAs. Although researchers have not yet understood the functions of lncRNAs in this disorder, there are several studies that have reported dysregulated expression of lncRNAs in correlation with the pathogenesis of ASD. In the current research, we evaluated the expression level of lncRNA, namely PCAT-1 in the peripheral blood of patients with ASD and healthy subjects.

Methods: This study was performed using peripheral blood samples of 71 children. The age range was from 4 to 15 years old. 30 children were diagnosed with ASD and 41 of them were healthy children. RNA extraction and cDNA synthesis were done on each blood sample. Forward and reverse primers were designed specifically for PCAT-1 lncRNA. For evaluation of expression levels of PCAT-1, Real-Time PCR was performed. Finally, Graph Pad Prism6 software was used for statistical analysis

Results: Our study showed that there is a significant difference between the amount of expression of PCAT-1 in children with ASD and healthy children (P value <0.0001). According to our investigations expression of PCAT-1 in ASD patients was 40 times lower than the healthy population. Specificity and sensitivity of PCAT-1 expression levels were investigated, using ROC Curve analysis; the results showed 0.843 erea under the curve (AUC), P value <0.0001, sensitivity =80%, specificity =70.73%, and cut off >6.067. These

results can propose the potential of using PCAT-1 as a diagnostic biomarker for ASD. In brief, our investigations showed that PCAT-1 expression levels in ASD patients were meaningfully downregulated in comparison with healthy children.

Conclusion: This study can provide clues for an association between reduced levels of PCAT-1 and ASD, as well as the possibility of using PCAT-1 as a diagnostic biomarker for ASD. Given that ASD patients generally are being diagnosed by behavioral symptoms such as social communications and interactions and up to now, there are no significant lab-based examinations to diagnose these cases; using long non-coding RNAs such as PCAT-1 as diagnostic biomarkers could be a milestone in diagnosis of ASD. Also because of the overlapping of some symptoms of ASD with combined psychiatric conditions, the possibility of false diagnoses is inevitable; but in the case of using PCA-1 expression as a biomarker, the chances of accurate diagnosis will elevate. Due to the limitations of this study, complementary investigations are needed to prove our findings and demonstrate the role of PCAT-1 in the pathobiology of ASD.

Keywords: Autism spectrum disorder, PCAT-1, lncRNAs, diagnostic biomarkers, gene expression

Dysregulation of TPO in a ceRNA network promotes anaplastic thyroid cancer: integrated gene expression profiling and systems biology analyses (Research Paper)

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Introduction: Anaplastic thyroid cancer (ATC) is an uncommon and the most aggressive malignancy of the thyroid gland with a high mortality rate. This type of cancer is most common in elderly people over the age of 60 years. Although this fatal abnormality makes up less than 2% of all thyroid cancer cases, the median survival of patients with ATC is about 5 months and less than 20% 1-year survival. Due to the immediate spreadability of the disease, an opportune diagnosis is critical. Therefore, determining reliable genetic biomarkers would improve the prognosis and treatment of ATC. The Competing Endogenous RNA (ceRNA) network hypothesis proposes that lncRNAs and mRNAs competitively bind to limited miRNAs through miRNA response element (MRE) to regulate the suppression or induction of gene expression. Thus this network could be used to construct a potential model for the diagnosis and treatment of ATC. The present study aimed to identify potential biomarkers and biological networks of gene interaction, including mRNAs, lncRNAs, and miRNAs, that have a remarkable impact on ATC progression.

Methods: In the first place, the Anaplastic thyroid cancer Microarray dataset (GSE33630) was extracted from NCBI Gene Expression Omnibus(GEO) to identify differentially expressed genes (DEGs) in ATC compared to normal thyroid samples. Subsequently, genes with significant decreases in expression regulation were analyzed by GEO2R. Further, expression analysis of elected gene was validated by GEPIA2 and ENCORI databases. According to the microarray data comparison between ATC and Normal tissue, the most significant gene with observable expression change was selected ($|logFC| > 2$ and adjusted p-value< 0.05). Furthermore, biological pathways were processed through KEGG and Reactome databases.Moreover, STRING database was utilized to find significant protein-protein interactions among our selected gene and related genes. In addition, miRWalk database was used to detect miRNA-mRNA interactions and find a significant miRNA. Finally, LncBase v.3 was employed to find an appropriate lncRNA that could complete

the network. Furthermore, LncRRIsearch was utilized to ensure that the chosen lncRNA is highly significant in Anaplastic thyroid cancer.

Results: The GEO data analysis of GSE33630 revealed that among all the 352 genes that showed downregulation, TPO was identified to be the most significant down-regulated gene in ATC samples compared to controls with adj.P.Val = 2.17E-27 and logFC = -7.3149612. The TPO gene provides instructions for biosynthesizing thyroid hormone and also it is known to be associated with thyroid gland diseases. According to the STRING database analysis, TG, IYD, FOXE1, and DUOX2, had the most significant protein-protein interactions with TPO. Moreover, Analysis of possible mRNA-miRNA interactions by miRWalk, demonstrated a significant connection between TPO and hsa-miR-769-3p that was confirmed by ENCORI co-expression analysis(p-value = 9.26e-03). Finally, H19 was identified as a considerable lncRNA using the LncBase v.3 database, which has a strong interaction with our selected miRNA.

Conclusion: Based on the results of this investigation, TPO plays an important role in thyroid hormone synthesis. Also, the down-expression of TPO in Anaplastic thyroid cancer could establish a novel ceRNA regulatory network among hsa-miR-769-3p, TPO, and H19 that could be suggested as potential diagnostic and prognostic biomarkers associated with Anaplastic thyroid cancer.

Keywords: Anaplastic thyroid cancer TPO ceRNA network Microarray analysis

Ebola Virus Disease: A narrative review (Review)

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Introduction: The Ebola virus (EBOV) belongs to the family Filoviridae, which is a group of single-stranded RNA viruses that can lead to severe hemorrhagic fever in humans and other primates. Six species of EBOV have been identified, including Zaire ebolavirus, Sudan ebolavirus, Tai Forest ebolavirus, Bundibugyo ebolavirus, Reston ebolavirus, and Bombali virus. In 1976, the disease emerged in two simultaneous outbreaks in Sudan and the Democratic Republic of Congo. Subsequently, it has caused intermittent outbreaks in several African nations. The West Africa Ebola outbreak between 2014 and 2016 was the largest, resulting in numerous cases and fatalities. The outbreak of Ebola virus disease (EVD) in West Africa in 2014-2016 emphasized the need for effective control and prevention measures.

Methods: A thorough search of the existing literature was carried out to collect pertinent articles related to EVD. Electronic databases such as PubMed, Google Scholar, and Web of Science were systematically explored using relevant keywords. The inclusion criteria encompassed studies that specifically examined different facets of EVD.

Results: Since 1976, the African continent has been confronted with a series of Ebola outbreaks, marking significant challenges in public health and necessitating urgent attention. The EBOV belongs to the Filoviridae family which comprises of filamentous and enveloped viruses with a single-stranded and negative-sense RNA genome. This virus is an infectious zoonotic pathogen characterized by its ability to quickly transmit between humans and non-human primates. This viral pathogen exhibits a wide range of cellular tropism, meaning it has the capacity to infect and replicate within various types of cells throughout the body however, the early targets appear to be immune cells. Ebola virus is primarily found in animal reservoirs, and several species of animals have been recognized as potential hosts. The natural

reservoir of the virus is believed to be fruit bats of the Pteropodidae family. This virus is transmitted through direct contact with the body fluids of infected animals or humans (e.g., blood, saliva, sweat, urine, feces, vomit, breast milk, semen, or other secretions). There are several modes of transmission of the EBOV, and understanding them is crucial to mitigate the virus spread. EVD is distinguished by symptoms such as fever, fatigue, muscle pain, headache, and hemorrhage however the severity of the disease is influenced by various factors, including the strain of the virus, the viral load, and the individual's immune response. Generally, there are three main methods used to diagnose EVD (I) serological tests (II) molecular tests and (III) Rapid Diagnostic Tests (RDTs). It is important to note that, Ebola not only affects physical health but also has psychological consequences, leading to emotional distress and long-lasting effects on survivors, families, and communities. Addressing the emotional impact requires a comprehensive approach, including psychological support and training for healthcare workers. While EVD presents significant challenges on its own, co-infection with other pathogens such as human immunodeficiency virus (HIV), malaria, and GB virus c (GBV-C) can further complicate diagnosis and treatment. Despite advancements and the identification of new treatments for EVD, the primary approach to treatment continues to be centered around providing supportive care. Early detection and supportive care can enhance the likelihood of survival. This includes intravenous fluids, electrolyte replacement, and treatment of secondary infections. Experimental therapies, for instance, monoclonal antibodies and antiviral drugs, have shown promising results in animal studies and some clinical trials. Some African countries have incorporated the utilization of vaccines created for Ebola Virus Disease (EVD); however, ongoing research is being conducted to assess their efficacy and long-term safety.

Conclusion: In conclusion, EBOV infection is a serious public health concern with devastating consequences. Early detection and treatment are essential to ensure that the virus does not spread and that affected individuals have the best chance of making a full recovery. It is also important to remember that the virus is preventable through proper hygiene and sanitation measures. With the right precautions, widespread outbreaks can be avoided.

Keywords: Ebola, Epidemic, Treatment, Coinfection, Symptoms

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Echinometrin peptide as biomarker of chronically salt-exposed sea urchin Echinometra mathaei. Toward an understanding of red cell degranulation under stressful condition (Research Paper)

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1.
2.

Introduction: Peptides are promising molecules that fill gaps in current therapeutic approaches, between small organic molecules (0.4–2 kDa) and protein drugs. It is thought that peptides signify a group of potential fascinating biotechnological molecules to be developed, regarding their specificity and high potency versus the (comparative) small size. Problems concerning their bio distribution and enzymatic degradation had dispirited their development as medicines, but these problems can now be avoided by using new constructions, encapsulation and/or injectable-solution. The marine echinoderms has previously provided molecules with therapeutic potential; therefore, they contain a good source of molecules that has been poorly discovered. Marine invertebrates produce/secrete/develop molecules for some purposes, including chemical defense against predators, oxidative stress and even ingestion, establishing a broad inventory waiting to be explored. Echinometra mathaei can be found throughout the Persian Gulf coast and are testified to be one of the major causes of marine coincidences on the shoreline. Although not lethal, these accidents are described to be exceedingly painful. Sea urchins have a large quantity of perivisceral coelomic fluid by which the internal organs seem to be protected. The survival of urchins in the contaminated marine environment is dependent on their ability to defend themselves against xenobiotics, micro biota and oxidative damages. These organisms have developed defense responses mainly based on immune cells and humoral elements contained in the coelomic fluid.

Methods: Sea urchins Echinometra mathaei were collected from Qeshm Island, Persian Gulf. The coelomic fluid (about 2 mL) was extracted from the sea urchin by puncturing the peristomial membrane and hypodermic needle. Mass spectrometry analyses were performed by a liquid chromatograph-triple quadrupole mass spectrometer (LC-QqQ-MS, Agilent G6410). The coelomic fluid of specimens was diluted in a 50% ACN containing 0.5% formic acid, and was directly introduced in the spectrometer, at a flow rate of 50 µL min−1, in positive ionization mode and mass spectra collected in the 50–2000 m/z range. The results were automatically processed by MS data, and then manually verified.

Results: In positive ionization mode, we detected dominant second order peptide ions of m/z = 353 [M+3H] 3+and m/z = 265 [M+4H] 4+, for molecular mass of 1054 Da, then the daughter ions spectra were explored and manually verified for accuracy and precision. The deduced sequence of the eight-residue peptide was LRKLMLQR.

Conclusion: The ion signal of m/z 1054 was attributed to protonated Echinometrin [M+2H] +2 besides it had been sequenced as LRKLMLQR. Echinometrin was firstly isolated from the peristomial coelomic fluid of Echinometra lucunter sea urchin, interestingly we deciphered Echinometrin in samples from outlet of Desalination plant. As mentioned earlier, we also observed pro-inflammatory reactions, such as red spherules recruitment or PHNQs release in some stressed specimens (personal observation). This cell recruitment may be caused by the presence and increased content of activated mediators, such as Echinometrin. Echinometrin as a cryptide peptide was primarily isolated from the peristomial coelomic fluid of E. lucunter, which is thought to be involved in stimulating the adaptive immune process related to stress by inflammatory feedbacks, such as , promoting histamine release, foot edema, white cell recruitment and depletion of the pain threshold. Likewise, it has been proved that Echinometrin from E. lucunter activate the in vivo degranulation of mouse mesenchymal MCs in a dose exposure mode, with pro-inflammatory effects.

Keywords: Echinometrin, Degranulation peptide, Sea urchin, Biomarker, Stress.

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Economic Perspective on Novel Cancer Treatment Method: Pathogen-Based Immunotherapy (Review)

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Introduction: Cancer is a global health challenge with significant social and economic impacts. This disease, characterized by abnormal cell growth and tumor formation, often requires treatments like surgery, chemotherapy, and radiation therapy, which carry their own drawbacks. Researchers are exploring innovative methods like immunotherapy, which uses pathogens (bacteria, viruses, parasites, and fungi) to activate the immune system against cancer cells. This article analyzes the economic implications of these treatments, especially immunotherapy, through analytical and statistical methods. It aims to provide insights for informed decision-making in cancer treatment, benefiting healthcare policymakers and stakeholders.

Methods: Various data collection methods were employed to thoroughly analyze the economic dimensions of innovative cancer treatments. About 250 articles, focusing on cancer treatment via immunotherapy using diverse pathogens (e.g., bacteria, parasites, fungi, viruses), underwent systematic review. These articles were systematically sourced from reputable references like Google Scholar and PubMed. Extracted data were integrated into the analyses, following a comprehensive approach encompassing methodologies such as: 1. Cost-Effectiveness Analysis (CEA): To compare costs and treatment effectiveness. 2. Cost-Benefit Analysis (CBA): For assessing economic value and monetary benefits. 3. Financial Impact Analysis: Examining financial consequences on healthcare and the economy. 4. Social Impact Analysis: Evaluating societal implications of improved cancer treatment through immunotherapy. 5. Cancer-Related Cost Accounting: Identifying and comparing costs directly linked to cancer treatment. This research provides an in-depth evaluation of cancer treatment's economic implications, focusing on immunotherapy.

Results: CEA provides a precise evaluation of the cost-effectiveness of different cancer treatments. Treatments that utilize various pathogens to enhance the immune system for cancer treatment often incur higher costs but yield notably positive outcomes, including enhanced patient quality of life, increased work and daily activity capacity, and economic efficiency through reduced healthcare expenditures. CBA reveals diverse economic advantages and disadvantages of cancer treatment using pathogens to boost immunotherapy. While initially costlier, the economic value of such treatments, stemming from improved patient quality of life, heightened societal productivity, and reduced costs related to treatment side effects, justifies investment. Financial Impact Analysis demonstrates that cancer treatments involving the use of pathogens for immunotherapy can lead to reduced expenses associated with ancillary treatments, hospitals, and emergency care. This cost reduction positively affects the healthcare system and the economy, promoting equitable resource allocation. Social Impact Analysis highlights significant improvements in patients' quality of life due to cancer treatments that employ pathogens for immunotherapy. These improvements enable patient reintegration into society and the workforce, contributing to the economic and social advancement of various regions. Accounting for Cancer-Related Effects Analysis underscores the notably high cancer-related costs, including treatment expenses. Cancer treatments utilizing pathogens for immunotherapy play a pivotal role in cost reduction and financial management improvement. Challenges and Considerations: 1. High Costs: Cancer treatments involving the use of pathogens for immunotherapy may have higher initial costs, posing challenges for patients and the healthcare system. Attention to cost management and increasing access is essential. 2. Personalization: Immunotherapy treatments that employ pathogens disrupt the standardization of treatments and focus on personalized interventions, presenting economic and managerial challenges. 3. Access and Limited Resources: Ensuring equitable access to cancer treatments involving the use of pathogens for immunotherapy and securing financial resources for these treatments are crucial challenges, demanding equitable resource allocation. 4. Need for Further Research: Advanced research is essential to enhance immunotherapy methods involving pathogens and improve their economic efficiency, mandating financial support.

Conclusion: This article delves into the economic perspective of pathogen-based immunotherapy, a novel approach to cancer treatment. Findings from various analyses highlight the potential of pathogen-based immunotherapy to improve patient quality of life, reduce treatment expenses, enhance productivity, and lower healthcare costs. However, these treatments have varying economic advantages and disadvantages, demanding careful management and improved accessibility. It is recommended that

policymakers and healthcare systems invest in and foster the development of these innovative therapies due to their positive economic effects on cancer treatment. Addressing the challenges outlined in this study is crucial for establishing an efficient decision-making framework in cancer treatment, benefiting public health and the economy.

Keywords: Immunotherapy Cancer Economics Treatment Cost

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Effect of Kojic Acid on the expression of virulence genes of Staphylococcus aureus (Research Paper)

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Introduction: Introduction: Staphylococcus aureus is one of the most significant human pathogens that causes various sorts of diseases and invasive infections. Recently, due to the resistance of this bacterium to several medications, it has become difficult to treat infections caused by it. The use of biological compounds to control infections might be a solution to this challenge. This study aimed to investigate the influence of Kojic acid on the expression of some virulence factors of S. aureus.

Methods: Materials and Methods: A total of 67 isolates of S. aureus that were collected from hospital sources, were identified and investigated by standard diagnostic and molecular techniques. Then, effect of Kojic Acid on the standard and isolated S. aureus strains was investigated. The expression levels of α-hemolysin and enterotoxin A genes were measured in the presence and absence of Kojic acid using a Real-Time PCR technique. The obtained data were analyzed using standard statistical methods in SPSS software (version 16) and Prism-GraphPad software. $P<0.05$ was considered statistically significant in the comparative data.

Results: Results: The results of the MIC of Kojic acid showed that the minimum concentration of Kojic acid that inhibits the growth of S. aureus was equal to 10 mM. As a result, the expression of hla gene was decreased 9-fold and the expression levels of sea gene was only decreased 2.7-fold.

Conclusion: Conclusion: In this study, the desirable effects of Kojic acid on S. aureus strains were observed. Due to the high inhibitory effect of the sub-MIC of Kojic acid on the expression of virulence factor genes in S.aureus, this compound could potentially reduce the virulence of S. aureus.

Keywords: key words: Staphylococcus aureus, Virulence factor, Gene expression, Kojic acid

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Effect of chemical compounds QM380 and QM381 on NLuc-NLRP3.pyd and CLuc-ASC purified proteins interaction (Research Paper)

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Introduction: NLRP3 is a cytosolic pattern recognition receptor that plays a crucial role in inflammatory responses to pathogens, danger signals, and other stimuli. Upon activation, NLRP3 forms an inflammasome containing the NLRP3 molecular sensor, the apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and pro-caspase-1, resulting in caspase-1 activation, release of proinflammatory cytokines named IL-1β and IL-18 and eventually pyroptosis. The broad involvement of the NLRP3 inflammasome in various inflammatory diseases such as multiple sclerosis, type 2 diabetes, and cancer makes it a highly attractive drug target. A range of pharmacological inhibitors of NLRP3 inflammasome has been previously described while no specific inhibitor exists for the various components of inflammasome complexs such as pyd domains of NLRP3 and ASC.

Methods: In this study, the split luciferase complementation assay was used as an approach to investigate interactions between the NLRP3-pyd and ASC. Both proteins were expressed in E.coli and purified by Ni-NTA-sepharose. The effect of two chemical compounds QM380 and QM381 on these homotypic interactions was checked by luciferase activity assay. The Firefly luciferase enzyme was used in a split form in that the pyd domain of NLRP3 is attached to one fragment and ASC is attached to another fragment forming NLuc-NLRP3pyd and CLuc-ASC respectively. Also, we applied molecular docking via autodock vina to better understand interactions between chemical compounds and our proteins.

Results: Both proteins were expressed, purified, and checked out by SDS-PAGE. Bioinformatics analysis demonstrated that QM380 interacts with approximately the second interface of the pyd domain which is less important among the other interfaces and also, QM381 is involved in the first and second interfaces. In vitro results show the effects of the chemical compounds on the purified proteins that QM381 in 3mM concentration inhibits 50 percent of interactions while QM380 did not affect these homotypic interactions confirming our bioinformatics analysis.

Conclusion: NLRP3 inflammasome is the most studied of the inflammasome family and plays a crucial role in the development of inflammatory diseases. In the past, cytokine therapy and antibodies were used for targeting IL-1β and IL-18 which led to an increased risk of infection and various side effects. Secretion of IL-1β and IL-18 is regulated by NLRP3 inflammasome, which targeting NLRP3 is a highly attractive strategy in curing inflammatory disease. According to this study, these chemical compounds have shown promising effects on homotypic interactions of pyd domains or could be a potential lead for further study.

Keywords: NLRP3-pyd, ASC, QM380, QM381

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Effect of docetaxel and celecoxib co-treatment on cell viability of human triple negative breast cancer cells (MDA-MB-231) (Research Paper)

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Introduction: Breast neoplasm is one of the most common malignancies. Among different types of breast neoplasm, triple negative breast cancer (TNBC) is more invasive, and survival with this type of cancer cells is less. The present study aimed to investigate the effects of combination treatment with docetaxel (DTX) and celecoxib (CLX) on the cell viability of triple-negative human breast cancer cells (MDA-MB-231).

Methods: In this in vitro study, MDA-MB-231 cell line were cultured in RPMI-1640 medium containing 10% FBS. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) test was performed on the cells to investigate the IC50 of DTX and CLX. Then cell viability percentage of MDA-MB-231 cells was evaluated after combination treatment with DTX and CLX at 24 and 48 hours.

Results: The estimated IC50 was 50.22 µM for DTX and 73.95 µM for CLX. The MTT results showed that DTX, CLX, and combined treatment significantly reduced cell viability percentage in 24 and 48 hours.

Conclusion: The results of this in vitro study showed that the concomitant use of DTX and CLX is effective in decline of cell viabilty percentage which might be effctive in decreasing of DTX dosage. However, further studies are needed in this field.

Keywords: Celecoxib, Docetaxel , MDA-MB-231, Triple Negative Breast Cancer.

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Effect of Dopamine Concentration on Polydopamine Nanoparticle Synthesis and Antioxidant Properties (Research Paper)

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Introduction: Polydopamine (PDA) has gained significant attention for its multifunctional properties in material science and biomedical applications. The polymerization of dopamine, a simple and versatile catecholamine, leads to the formation of PDA coatings on various surfaces. Understanding the relationship between PDA synthesis conditions, particle characteristics, and antioxidant properties is crucial for harnessing its potential in biomedical and environmental applications. In this study, we investigate the synthesis of PDA at varying dopamine concentrations and its subsequent antioxidant capabilities.

Methods: Polydopamine was synthesized under controlled conditions at 37°C for three days with different dopamine concentrations (0.04 mg/ml, 0.16 mg/ml, 0.64 mg/ml, and 1.9 mg/ml). The antioxidant properties of each PDA sample were evaluated using UV-Vis spectrometry and a ROS scavenging test based on the Fenton reaction. ROS clearance percentages were calculated for each concentration, and the physical characteristics of the PDA nanoparticles were analyzed through sedimentation observations and particle size measurements.

Results: Our results revealed a concentration-dependent synthesis of PDA. Lower dopamine concentrations led to faster polymerization, resulting in smaller and lighter nanoparticles with no observable sedimentation. Conversely, higher dopamine concentrations produced larger and heavier particles, accompanied by sedimentation. Interestingly, the antioxidant effect of PDA exhibited a positive correlation with dopamine concentration. At the lowest concentration (0.04 mg/ml), ROS clearance was 29%, and at 0.16 mg/ml, it increased to 30%. Substantially higher ROS clearance rates were observed at the higher concentrations, reaching 80% at 0.64 mg/ml and 75% at 1.9 mg/ml. This suggests that PDA synthesized at higher dopamine concentrations possesses enhanced ROS scavenging capabilities.

Conclusion: In summary, our study demonstrates that the concentration of dopamine during PDA synthesis significantly influences both the physical characteristics of the nanoparticles and their antioxidant properties. Lower dopamine concentrations favor faster polymerization, yielding smaller, lighter PDA nanoparticles without sedimentation. In contrast, higher dopamine concentrations result in larger, heavier particles accompanied by sedimentation. Notably, the antioxidant effect of PDA increases with higher dopamine concentrations, indicating its potential as an efficient ROS scavenger. These findings provide valuable insights into tailoring PDA properties for specific applications, such as drug delivery, tissue engineering, and environmental remediation.

Keywords: Polydopamine, ROS scavenging, antioxidant properties, nanoparticle synthesis

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Effect of Ivermectin on The Induction of Apoptosis in HepG2 Cell Line (Research Paper)

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Introduction: Liver cancer is ranked third in the causes of cancer mortality around the world. Liver cancer poses a substantial public health issue due to its profound influence on our well-being. The development of sustainable and dependable approaches for preventing and treating liver cancer necessitates fundamental research into its molecular mechanisms. Cell lines serve as in vitro counterparts of tumor tissues, rendering them indispensable for fundamental research into the cancer nature. Ivermectin is a wide range acting drug used against several disease types including cancer. The present study aimed to investigate the effect of ivermectin on HepG2 liver cancer cell line.

Methods: HepG2 cells were cultured in DMEM medium containing 10% FBS and treated with 0.2, 0.4, 0.8, 1.5, and 8 µM concentration of ivermectin. After 72 hours they were evaluated by MTT assay for their viability. For studying the morphology of cells, Giemsa and invert microscopy were used. The expression of apoptotic genes, Bax, Bad, and Bcl-2, was also evaluated by real-time PCR. All data were analyzed using SPSS version 27.

Results: MTT assay showed the IC50 of ivermectin to be 0.4 µM. Peak apoptotic effect was recorded on the 8 µM concentration, which eliminated 90.5% of HepG2 cells. In the results of PCR, elevation of Bax and Bad genes and reduction of Bcl-2 gene were evident.

Conclusion: The present study showcased the apoptotic anti-tumor activity of ivermectin against HepG2 cell line. This can suggest the use of ivermectin against liver cancer, but more studies will be needed for further investigation.

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Keywords: Ivermectin, HepG2 cell line, Apoptosis, PCR, MTT

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Effect of lifestyle modification on menopause symptoms: A systematic review study (Review)

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Introduction: Menopause is a significant change in women's mid-life that comes with various symptoms. These symptoms vary and negatively affect their quality of life, including vasomotor, physical, and physiological problems. There are a large number of studies that suggest the effects of lifestyle modifications on the reduction of menopausal symptoms.

Methods: The research strategy involved general and specific English and Persian terms of menopause and lifestyle modifications with all possible search combinations. A review was conducted on studies that were published between 2000 to 2023 and that were indexed in the English databases PubMed, Scopus, Web of Science, and Persian databases Iran Medex, SID, and Magiran

Results: In total, (3 Cross-sectional, 5 Clinical trials) were included based on the study criteria. All studies were evaluated based on the STROBE index. Our analysis showed that lifestyle modifications could help reduce menopausal-related symptoms such as osteoporosis risk, obesity-related morbidity, and urogenital and vasomotor problems. There was one study that suggested there is no relationship between walking and menopause symptoms.

Conclusion: The results of most studies showed a positive relationship between lifestyle modifications and menopause. While a study has reported conflicting results. Therefore, it is highly recommended that further studies should be conducted in this area.

Keywords: menopause, lifestyle modification, menopause symptoms

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Effect of mitoquinone, resveratrol, and astaxanthin on the developmental potential of vitrified mammalian oocytes (Review)

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Introduction: Oocyte vitrification is an established method for female fertility preservation during reproductive age. Vitrification increases reactive oxygen species (ROS), depletes ATP, and induces apoptosis in oocytes, all of which have a harmful effect on the mitochondrial membrane potential (ΔΨm) in oocytes. Antioxidants improve the developmental potential of the vitrified oocytes. It suggests that vitrification might require more advancement. This review will focus on antioxidants, such as astaxanthin(Ax), resveratrol, and mitoquinone (MitoQ).

Methods: In this review, the English keywords cryopreservation, oocyte, fertility, astaxanthin, resveratrol, and mitoqunine, as well as their Persian equivalents, were searched in the Persian database of Magiran as well as the English databases of Pubmed, Elsevier, Web of Sciences, and the Google Scholar search engine between the years 2010 and 2022. Numerous quantitative and qualitative studies that shared the same topics as the current study were chosen and assessed.

Results: 22 studies that were more closely relevant to the objective of the current study were chosen. The results of the review showed that MitoQ, RES, and Ax enhanced survival and ΔΨm of vitrified oocytes under treatment. They also demonstrated that the blastocysts from vitrified oocytes had higher mean cell counts when added antioxidants. By reducing the levels of ROS and raising the levels of glutathione (GSH), these measures lessened the oxidative stress of vitrified oocytes, reduced the incidence of abnormal meiotic spindles, and improved the aberrant mitochondrial distribution pattern. They significantly improved the survival rate of vitrified oocytes and enhanced the blastocyst production of fresh and vitrified oocytes. Furthermore, vitrified

oocytes had a significantly increased relative fluorescence intensity of lysosomes, which the treatment was able to reduce. In vitrified oocytes, antioxidant treatment increased the mRNA levels of GDF9, SOD2, NRF2, and ATG5 in fresh and vitrified oocytes. The Bax/Bcl2 ratio and caspase3 mRNA expression was also considerably reduced in treated oocytes.

Conclusion: According to the results, using RES, Ax, and MitoQ may be useful for enhancinge the developmental potential of vitrification. This review showed that antioxidants might reduce cryopreservation damage during the vitrification of mammalian oocytes.

Keywords: oocyte, Vitrification, Antioxidant, Astaxanthin, Resveratrol, Mitoquinone

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Effect of Polycaprolactone/Carbon nanotube scaffold implantation along with liposomal ellagic acid in hippocampal synaptogenesis after spinal cord injury (Research Paper)

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3.

Introduction: Memory and cognition impairments are the most important secondary effects of spinal cord injury (SCI) in the hippocampus. Therefore, the present study aimed to examine the effect of implantation of polycaprolactone/ functionalized multiwall carbon nanotube (PCL/f-MWCNT) scaffold along with ellagic acid loaded liposome (EA@lip) in neurological function recovery and hippocampus deficit after SCI.

Methods: Twenty-four female Wistar rats were randomly assigned into 4 groups (n=6): Ctrl- group (laminectomy without SCI), Ctrl+ group (SCI), PCL/CNT group (implantation of PCL/f-MWCNT scaffold) and PCL/CNT/EA group (implantation of PCL/f-MWCNT/EA@lip scaffold). The injury model was the dorsal hemisection at the T9 level. Characterization of EA@lip made by remote loading method was done by transmission electron microscopy and dynamic light scattering. Also, the morphology of PCL/f-MWCNT fibers was investigated by field-emission scanning electron microscopy (FE-SEM). Behavioral tests were used to evaluate the neurobehavioral performance of the animals. After 4-weeks, excitatory postsynaptic potential was recorded from the CA1 area of the hippocampus. Hippocampal mRNA levels of amyloid beta precursor protein (APP), cyclic nucleotide phosphodiesterase (CNP), glutamate ionotropic receptor kainate type subunit 2 (GRIK2) and syntaxin-binding protein 1 (Munc 18-1) were assayed using reverse transcription-quantitative polymerase chain reaction (RT-qPCR).

Results: We demonstrated that, after implanting the PCL/CNT scaffold with or without EA@lip, the hippocampal action potential improved by increasing the slope and amplitude of fEPSP compared to the Ctrl+ group. RT-qPCR data showed that the expression of CNP and Munc 18-1 increased, and the expression of APP and GRIK2 decreased, in the groups that received

PCL/CNT with or without EA@lip compared to the injury group. We also proved that the treatment with PCL/CNT/EA@lip improved behavioral performance compared to the Ctrl+ and PCL/CNT groups.

Conclusion: This study demonstrated that PCL/f-MWCNT/EA@lip scaffold implantation improves functional potential and alters the expression of memory-related genes in the hippocampus post-injury.

Keywords: Action potentials, Drug delivery systems; Tissue engineering; Memory; Neurogenesis

Effect of Sperm Cryopreservation on miRNAs Expression and their correlation with sperm parameters in oligoasthenoteratozoospermia men (Research Paper)

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Introduction: Although sperm cryopreservation is a common method to preserve fertility, it may affect the spermatogenesis and male infertility by changing the expression of miRNAs transcripts. The aim of this study was to investigate the relationship between the expression of miRNAs 34c (mir 34C) and miRNAs 15b (mir15b) with sperm parameters in infertile oligoasthenoteratozoospermia men during the sperm freezing-thawing process.

Methods: In this experimental study, 25 semen samples in terms of oligoasthenoteratozoospermia parameters were collected from individuals referred to infertility treatment Center Qom. Each sample was divided into two, non-frozen (Fresh) and frozen groups. After rapid freezing and three-day storage in liquid nitrogen, samples were thawed in tap water and incubated for 2 hours in a CO2 incubator. Sperm parameters were evaluated using WHO criteria. The expression level of miRNAs (34c and 15b) was assessed by Real-time PCR technique. The results were analyzed by repeated measures ANOVA and the difference was considered significant at the level (p<0.05).

Results: The expression of miRNAs 34c decreased and miRNAs 15b increased significantly in the frozen group compared to the fresh group (P≤0.05). There was a significant decrease in sperm concentration, total motility and morphology in the frozen group compared to the fresh group (P≤0.05). A decrease in the level of GPx, SOD and TAC and an increase in the level of MDA and DNA fragmentation were observed during the freeze-thaw process in oligoasthenotratozoospermia. (P≤0.05). Sperm concentration, motility and morphology as well as oxidative stress factors and DNA integrity were correlated with the expression level of miRNAs (34c and 15b) (P≤0.05).

Conclusion: Our study suggested that cryopreservation of sperm can change the expression of miRNAs that can be involved in sperm quality. These non-

coding RNAs may be considered as fertility biomarkers for developing freeze-thaw strategies.

Keywords: Sperm, miRNAs, Cryopreservation.

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Effect of tumor-associated macrophages on drug resistance in cancer (Review)

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Introduction: Cancer is always one of the major public health problems around the world. Breast, lung, and colorectal cancer are among the most common cancers, and liver, lung, and stomach cancer are among the deadliest cancers. Cancer is actually a complex disease that is caused by many reasons and is a multifactorial disease. Meanwhile, the tumor microenvironment contains things that affect cancer and its process. This environment contains various cells, including macrophages, which can affect cancer and its metastasis.

Methods: This is a review study Collected by reviewing articles related to tumor-associated macrophages and their effect on Cancer with the keywords " tumor-associated macrophages " OR "TAMs" and "cancer" from 2020 onwards, from Google Scholar and Pubmed it has been compiled and written. 35 articles were collected, of these 7 articles were excluded because of lack of subject relevance, and only 28 studies were used. The inclusion criteria were all articles that examined the effect of tumor-associated macrophages on Cancer.

Results: The review of various studies showed that the interaction between TAMs and cancer stem cells occurs through IL6/STAT3, hedgehog, NF-KB, and IL10/STAT3/bcl2 signaling pathways. TAMs play a role in the release of cytokines, effect on EMT, participation in metabolic reprogramming and release of chemokines, and ultimately affect drug resistance in cancer.

Conclusion: TAMs are an important part of the tumor immune microenvironment and play an important role in the growth, progression, and drug resistance of cancer. Finally, it shows that TAMs can be a suitable target for reducing drug resistance in cancer, and by working on them, the effectiveness of drugs in people with cancer increased.

Keywords: Tumor-associated macrophages (TAMs), Drug-resistant, Cancer

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Effect of Variant and Drug Based on ID (Research Paper)

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Introduction: Genetic polymorphism is defined as the inheritance of a trait controlled by a single locus with two alleles, the frequency of the lowest alleles being: about 1% or more is one of the most important inherited polymorphisms known to affect the digestive system and drug response. Polymorphism of oxidation of debrisoquine type (CYP2D6). The disclosure of CYP2D6 polymorphism in the pharmacogenomics section of clinical pharmacology created modern attractions. Disease, heart failure, and atrial fibrillation Metoprolol is listed by the US Food and Drug Administration (FDA) as a relatively sensitive substrate for clinical drug-drug interaction (DDI) studies because it is primarily metabolized by cytochrome P450 2D6 (CYP2D). According to past studies, researchers in different countries found CYP2D6*1 variant, which is related to the drug metoprolol, and research was conducted on this drug, which is seen in heart failure.

Methods: From 500 next-generation sequencing samples, CYP2D6*1 allele were analyzed. This variant is associated with the drug metoprolol and is seen in heart failure, therefore, the CYP2D6*1 allele is assigned as a normal function allele by CPIC.

Results: The CYP2D6 quality is profoundly polymorphic in the allele frequency of rs16947 from 4 genome aggregation databases Genome, gnom AD Exome, 1000genomes, ALFA, gnom AD, the information of alleles based on the whole population or separately for each country was expressed as a percentage, which the gnom AD Genome database separately according to the analysis that was done From a total of n=40,724 in African and American population, A allele is 51.69% and G allele is 48.41% and 1000 genomes database from a total of n=1,322 in African and American population, A allele is 55.37% and G allele is 344.6% and ALFA database or based on data The allelic frequency collectors reported 33.98% of A allele and 66.02% of G allele from a total of n=1,904

Conclusion: The aim of this study is to associate a variant based on its ID and association with the target drug using the PharmGKB database, which is a knowledge base that shows the relationships between drugs,

diseases/phenotypes, and genes involved in pharmacokinetics (PK) and It shows pharmacodynamics

Keywords: Cytochrome P450, Genetic polymorphism, Metoprolol drug, PharmGKB database

Effective Factors on Depression in Breast Cancer Women (Review)

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Introduction: Depression is a common psychiatric complication in women with breast cancer. Reviewing the literature indicates that there are various factors affecting on depression; hence, this study aims to investigate the effective factors on depression in breast cancer women.

Methods: In this review, the author applied Google Scholar, SID, Magiran, Science Direct, Scopus and PubMed by suitable keywords from 123 related articles, referred to years 2000 - 2022. Finally, 36 studies were selected to write this review study.

Results: The findings were classified in 5 main levels: Demographic factors including (lower age, illiteracy and cancer background in family), medical factors including (stage of disease, type of medication –especially chemotherapy and Mastectomy , hormonal drugs like Tamoxifen, side effects of medication on sexual function, menstruation and fertility), psychological factors including (fear of relapse and death, disappointment, mala-daptive coping strategies and attitudes, depression and mental disorder history, depression background in family, body image disorder), socio-economic factors including (lower income, family problems and lack of social and emotional support by spouse, family, friends and treatment team) and spiritual-religious factors including (low spiritual-religious believes). Reviewing

the articles indicates that these factors can increase the risk of depression in patients with breast cancer.

Conclusion: As psychological and social factors are significantly related to depression prevalence in women with breast cancer, it is suggested to edit necessary programs and consultations to remove the factors and improve women's health, by health service providers.

Keywords: depression, breast cancer, effective factors, psychological factors, demographic factors

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Effective parenting interventions: A review study (Review)

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Introduction: Parents are often concerned about how to treat their children properly and these concerns can be alleviated with appropriate interventions. The purpose of this study is to review the effective interventions on parenting.

Methods: This study was a review method. Gather information in SID databases , Pub Med, Scopus, Google scholar, Web of Science and search with the keywords "Children's health", "Parenting styles" "Effective interventions" and their Persian equivalents in the period 2005 to 2022. At the end of the 75 articles searched, 12 articles related to the purpose were reviewed.

Results: The findings of this study were classified into two groups of educational and psychological interventions. In the educational category, interventions improve parenting by providing an educational program based on increasing awareness (causing change in parents' awareness, attitude and practice). And the psychological category includes interventions: play therapy, mindfulness, cognitive-behavioral therapy, schema therapy.

Conclusion: The study indicates that educational and psychological interventions can have positive effects on parenting. And lead to improved relationships between parents and children.

Keywords: Parenting, effective interventions

Effectiveness of adequate sleep in reducing stress and anxiety in cancer patients (Review)

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Introduction: A two-way relationship between sleep and cancer. People with cancer are disproportionately affected by sleep disorders and insomnia. These problems can lead to psychological and behavioral effects that delay the diagnosis and treatment of cancer. In addition, sleep as a form of guided meditation is effective in reducing stress and anxiety in patients with cancer. Effective techniques and other methods can be used in this nonpharmacological intervention. Studies have shown that these methods can increase the quality of life of patients with cancer and help reduce injuries, complications, and physical and mental health. By including sufficient sleep in patients ' treatment plans, they can help reduce stress and anxiety. This study investigated the relationship between adequate sleep and reduction in stress and anxiety in patients with cancer.

Methods: this study was conducted using a narrative review method. After studying and evaluating 80 original articles and review systems in international databases and websites: PubMed, Sid, Scopus, Google Scholar, and ISI, and through an advanced and extensive search using the keywords "cancer", "sleep", "stress", "exercise" During the years 2014 to August 2023, among these retrieved articles, 35 selected articles were identified and examined in the stages of title, abstract, and full text.

Results: Adequate sleep is important for overall health and well-being. Especially for cancer patients who may face more stress and anxiety. For cancer patients, sleep is critical for managing symptoms and improving their quality of life. However, many cancer patients suffer from disorders and insufficient sleep because of pain, treatments, and psychological distress. Lack of sleep can aggravate symptoms and increase stress and anxiety levels. Adequate sleep can improve cancer patients in various ways, including physical and mental fatigue, increasing pain tolerance, and improving performance. Therefore, healthcare providers should encourage cancer patients to prioritize sleep and provide them with strategies to improve sleep quality.

Conclusion: Prioritizing sleep as an intervention for cancer patients undergoing treatment is the responsibility of the healthcare provider. By adopting sleep habits and receiving support from their healthcare team, patients with cancer can experience improvements in their stress and anxiety levels.

Keywords: cancer, sleep, stress, anxiety

Effects of Aerobic and Interval training on G6Pase expression in The hepatocytes and Fasting Glucose in Type-2 diabetic rats (Review)

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Introduction: Type 2 diabetes is a general health problem in the world, with complications that place a heavy burden on the public health system. Increased production of glucose in the liver is responsible for increasing fasting blood glucose and an important part of glucose uptake after eating a meal in diabetic people. Insulin controls the production of glucose in the liver by controlling the expression of two G6Pase enzymes and PEPCK , involved in the gluconeogenesis process (1). These enzymes are regulated by PGC-1α (2). G6Pase is one of the key enzymes involved in gluconeogenesis that converts glucose 6 phosphate to glucose. The presence of this enzyme allows the tissue to release glucose into the blood. Glucagon and Insulin regulates the expression of PGC-1α, thereby controlling the transcription of G6Pase (3). On the other hand, exercise is generally recommended because of the beneficial effects on glucose control in the treatment of T2D (4). Exercise improves insulin function and glucose hemostasis and insulin sensitivity (5). However, further studies are needed to evaluate in detail the relative effect of exercise. Therefore, identifying the effect of exercise training on hepatic gluconeogenesis in diabetic patients and how to regulate the genes involved in it, is an undeniable necessity to find a milestone in helping to reduce diabetes complications. In the present study, the effect of 10 weeks of Aerobic and Interval training on the expression of G6Pase gene in the liver of diabetic rats was investigated.

Methods: The present research was done on male Wistar rats. The sample consisted of 24 rats in a 10-week-old age range of 220 (± 20) grams, selected randomly. First, type 2 diabetes was induced by intraperitoneal injection of nicotine amide and streptozotocin in the subjects (6). To ensure diabetic rats, 72 hours after diabetes induction, fasting blood glucose was measured and blood glucose above 250 mg/dl, It has been considered as a criterion for ensuring that rats develop type 2 diabetes (7). After type 2 diabetes induction,

the samples were divided into Three groups of Aerobic, Interval and Controlled. The training program was 10 weeks and five times a week, with a gradual increase in speed (8, 9). 48 hours after the last training session, liver tissue samples were taken after an overnight fast. Fasting glucose, serum insulin, insulin resistance, G6Pase gene expression in hepatocyte were measured in All three groups. After confirming the normal distribution of data with Shapiro Wilk test and homogeneity of data with Levene's test, One-way analysis of variance (ANOVA) along with the LSD follow-up test was used to compare the means of the indices. Data were analyzed using SPSS software version 22 at the significant level of 0.05.

Results: Based on the results obtained, the blood glucose level in the Aerobic and interval diabetic groups was about 27.9% and 26.3% lower than the control group, respectively and the results of the ANOVA showed a significant difference between the blood glucose levels in the Aerobic and interval diabetic groups compared to the diabetic control group ($P < 0.0001$). Also, the level of blood insulin in the Aerobic and interval diabetic groups was about 28.5 and 27.3% higher than the control group, respectively and 10 weeks of interval training significantly increased the level of serum insulin in the Aerobic and interval diabetic groups compared to the diabetic control group ($P < 0.0001$). Insulin resistance respectively was about 7.47% and 6.6% lower in the Aerobic and interval diabetic groups than in the diabetic control group. Despite the decrease in insulin resistance in the Aerobic and interval diabetic groups compared to the control group, this decrease was not significant ($P = 0.226$). G6Pase gene expression respectively increased by 37% and 24% after 10 weeks of Aerobic and interval exercise in Aerobic and Interval diabetic groups compared to diabetic control group. Based on ANOVA, there was no significant difference between groups in G6Pase gene expression ($P = 0.551$). In other words, 10 weeks of Aerobic and interval trainings did not affect G6Pase gene expression in type 2 diabetic rats.

Conclusion: In this study, the effect of 10 weeks of Aerobic and Interval trainings on G6Pase in liver, glucose and insulin tissues in T2D rats was studied. The results of this study showed that Aerobic and Interval trainings led to a significant decrease in glucose and a significant increase in serum insulin level in T2D rats,but there was no significant difference between groups in G6Pase gene expression. Based on the available evidence regarding the increase in hepatic glucose production and the process of gluconeogenesis as an important pathological factor in diabetic patients, aerobic and interval activity probably leads to a decrease in gluconeogenesis with an increase in insulin levels and ultimately a decrease in glucose production, According to the results of this study, this glycemic regulation,

control and improvement of values Blood glucose and insulin have been tested without affecting G6Pase gene expression. However, given the limited research on the cellular and molecular domain of diabetes and under the influence of different types of exercise training with different intensities, and because of the limited scope of the present study, further laboratory and field studies are needed to elucidate other mechanisms.

Keywords: Aerobic exercise, Interval exercise, G6Pase, Type 2 diabetic

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Effects of Busulfan on Testis Tissue and Epididymal Sperm of Adult Mice: A Comprehensive Review (Review)

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Introduction: Busulfan, a chemotherapeutic agent widely employed in clinical settings, has been associated with detrimental impacts on male reproductive health. This comprehensive review aims to provide an in-depth analysis of the existing literature on the side effects of busulfan treatment on testis tissue and epididymal sperm in adult mice. Understanding the mechanisms and consequences of busulfan-induced damage to the male reproductive system is of paramount importance in addressing potential reproductive concerns in patients undergoing chemotherapy.

Methods: A systematic search of scientific databases, including PubMed, Scopus, and Web of Science, was conducted to identify relevant studies published until September 2023. The eligibility criteria for inclusion encompassed research focusing on the effects of busulfan on testis tissue and epididymal sperm in adult male mice. The review rigorously evaluated methodological aspects such as busulfan dosages, administration routes, treatment durations, and the assessment tools used to gauge testicular and sperm damage.

Results: Numerous investigations have shed light on the adverse effects of busulfan on the male reproductive system. The findings consistently demonstrate that busulfan, even at clinical doses, induces significant damage to testis tissue. Histological examinations reveal pronounced alterations, including disruption of seminiferous tubules, germ cell depletion, and impaired spermatogenesis. These detrimental effects are accompanied by an increase in apoptotic markers within the testicular tissue. Moreover, busulfan treatment has a substantial impact on epididymal sperm quality. Studies consistently report a reduction in sperm count, motility, and viability following busulfan exposure. Notably, this damage occurs at low doses of busulfan, suggesting a heightened vulnerability of sperm cells to the drug's cytotoxic effects. The compromised sperm quality is further underscored by an increase in DNA

damage, chromatin abnormalities, and elevated oxidative stress markers in epididymal sperm.

Conclusion: This comprehensive review underscores the deleterious consequences of busulfan treatment on testis tissue and epididymal sperm in adult mice. Busulfan, even at clinical doses, leads to significant histopathological alterations in testis tissue, characterized by seminiferous tubule disruption and germ cell loss. The drug's cytotoxic effects extend to epididymal sperm, resulting in reduced sperm count, motility, and viability. Additionally, the induction of DNA damage, chromatin abnormalities, and oxidative stress in sperm highlights the multifaceted nature of busulfan's impact on male reproductive health. The findings from this review emphasize the importance of careful consideration of the potential reproductive consequences of busulfan treatment in clinical settings. Furthermore, they underscore the need for developing strategies to mitigate busulfan-induced testicular and sperm damage, especially in individuals of reproductive age undergoing chemotherapy.

Keywords: Busulfan, testis tissue, epididymal sperm, cytotoxicity, apoptosis.

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Effects of common treatments on cancer incidence in multiple sclerosis patients (Review)

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Introduction: Multiple sclerosis (MS) is a condition that affects the central nervous system and is characterized by immune system involvement. An issue that poses significant challenges and concerns for individuals with multiple sclerosis is the development of cancer, which complicates their treatment and overall health condition. The occurrence of the cancer in the multiple sclerosis population is influenced by a range of factors. Numerous studies have explored this subject, and in this review article, our focus is to elucidate the correlation between these treatments and the cancer.

Methods: This review article was conducted by examining various articles focusing on the correlation between common treatments for multiple sclerosis patients and the occurrence of cancer. The articles were collected from 2010 onwards using the keywords "cancer" AND "multiple sclerosis" from the Pubmed database. A total of 84 articles were gathered, out of which 20 were excluded due to their lack of relevance to the subject matter. Therefore, only 64 studies were considered for the review.

Results: The association between commonly used treatments for multiple sclerosis (MS) and cancer has been evaluated through the reviewed articles. Immunomodulatory and immunosuppressant treatments, such as fingolimod, beta-interferon, dimethyl fumarate (DMF), cladribine, cyclophosphamide, natalizumab, pembrolizumab, alemtuzumab, rituximab, azathioprine, which belong to a group of treatments known as disease-modifying therapies (DMT), as well as cytotoxic drugs, have been examined and analyzed.

Conclusion: According to the reviewed articles, the likelihood of cancer in individuals with multiple sclerosis (MS) who undergo common therapies appears to vary depending on the specific treatment used. Some treatments have been found to increase the risk of cancer, while others have been associated with a decreased risk. However, certain treatments show no significant association with either an increased or decreased risk of cancer. However, the available evidence is limited, and further investigation is needed to draw more definitive conclusions.

Keywords: multiple sclerosis, cancer, treatment

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Effects of copper sulphide nanoparticles as a radio-sensitizer agent on colorectal cancer cells (Research Paper)

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Introduction: One of the greatest challenges in radiation therapy (RT) is the side effects of high doses due to considerations of adjacent healthy tissue radiation tolerance. In addition, radio-resistance of cancer cells is a major issue in radiation therapy. Consequently, it would be significantly important to develop new approaches to enhance the treatment efficacy. Here, we examined the potential of Fe3O4@Cus-PEG nanoparticles as a radiosensitizer agent.

Methods: Nanoparticles were synthesized and characterized for hydrodynamic diameter, morphology, and X-ray diffraction. MTT assay was used to evaluate the cytotoxicity of nanoparticles on colorectal cancer cell lines. To evaluating the in vitro radio-sensitization effects of the synthesized nanoparticles, colorectal cancer cells were treated with ionizing radiation and nanoparticles. The cytotoxic effects of different treatments were assessed by the MTT assay, reactive oxygen species analysis, and quantitative real-time PCR (q-RT PCR) assay.

Results: Our in vitro assays demonstrated that the intracellular hydrogen peroxide concentration and the expression level of Bax and Caspase-3 genes significantly increased in the cells treated with the combination of nanoparticles and radiation. Whereas, the expression level of the Bcl-2 gene in the combined treatment significantly decreased compared to the radiation alone. The combination index (CI) values for the combined treatments of nanoparticles and X-ray radiation at doses of 2, 4, and 6Gy were equal to 0.88 ± 0.03, 0.73 ± 0.3, and 0.67 ± 0.02, respectively.

Conclusion: This study suggests that Fe3O4@Cus-PEG nanoparticles can be used as a promising nano radio-sensitizing agent

Keywords: Colorectal cancer, Radiosensitizer, Ionizing radiation, Copper, Magnetite nanoparticles

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Effects of estrogen hormone on Rheumatoid Arthritis (Review)

zohreh yarahmadi,[1,*]

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Introduction: Rheumatoid Arthritis is a long-term and progressive autoimmune disease which causes inflammation and swelling and pain in the joints and other organs of the body. The common symptom of this disease includes joint stiffness which usually reaches its peak in the morning when waking up and gradually decreases with the start of daily activities. According to the research, women are more affected by rheumatoid arthritis than men. In this article, the effect of estrogen hormone on rheumatoid arthritis has been tried to be investigated.

Methods: Some research shows that hormones may play a role in aggravating or Relieving arthritis. For example, changing the level of estrogen hormone has effects on RA disease. Menopause can be mentioned as an example of the effect of estrogen on RA. In women, when the level of estrogen decreases drastically, they enter the menopause period. When a woman lives with a chronic disease such as rheumatoid arthritis, it may worsen during menopause. Another evidence is the effect of estrogen on arthritis during pregnancy (when the level of estrogen increases). According to a study carried out in 2019, it has been shown that 60% of women experience a decrease in RA symptoms during pregnancy but after childbirth (that is, when the level of hormones such as estrogen decreases), the occurrence of disease or exacerbation of RA has been observed in 46% of them. Also, RA patients witnessed the worsening of their disease symptoms in the days before menstruation, when the amount of estrogen in the body decreases. In a clinical study performed in June 1983, the daily examination of symptoms during 69 menstrual cycles in 14 patients with RA shows that rheumatoid arthritis has decreased in the post-ovulation stage of the menstrual cycle when we see the rise of estrogen

Results: With this evidence, we may conclude with further investigations in the future that Estrogen has a protective role in rheumatoid arthritis.

Conclusion: With this evidence, we may conclude with further investigations in the future that Estrogen has a protective role in rheumatoid arthritis.

Keywords: Effect of hormones on rheumatoid arthritis The effect of estrogen hormone on rheumatoid arthritis

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Effects of nanofibers properties on cell behavior (Review)

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Introduction: One of the materials that is currently being researched the most in the medical and tissue engineering fields is nanofibers. They have been put to use for things like cell culture, scaffolds and dressings for tissue engineering, drug delivery systems, and the immobilization of enzymes. The main component of tissue engineering for damaged tissue is scaffolds. They are also necessary for cell survival and function as well as for in vivo and in vitro tissue regeneration. Therefore, important factors in tissue engineering nanofibrous scaffolds include their architecture, pore density and size, morphology, surface adhesion, biocompatibility, and mechanical properties when in contact with body environment [1]–[5]. Polymer nanofibers are synthesized by various methods such as phase separation [6], self-assembly [7] and electrospinning [8]. Electrospinning, however, is a simple, economical and direct method for producing nanoporous scaffolds 63. In the electrospinning method, a high voltage electric field is responsible for the movement of the polymer jet from the tip of the needle that is connected to the source of the polymer solution [9]. With this method, nanoporous scaffolds of polymer biocomposites can be produced with the obtained nanofibers. High surface-to-volume ratio and high porosity are among the advantages of electrospun scaffolds, in which the nanostructure can be changed according to the need by changing parameters such as flow rate, voltage, the distance between the tip of the needle and the collector, and the polymer itself. The porosity and large area of nanofibers lead to more cell proliferation and as a result, it is a promising option for tissue engineering. In addition, these fibrous scaffolds have nanoscale properties and topographies similar to natural extracellular matrix (ECM), which stimulate cell proliferation and differentiation [64]. Cells interact with ECM or biomaterials [10], [11]. The physical characteristics of the substrate of cells are recognized by their surface receptor proteins and are converted into a series of biochemical signals in the cell [12]–[14]. Cell behavior in the case of nanofibers is proportional to some factors, some of which are mentioned in this paper.

Methods: This review article aims to demonstrate the behavior and response of cells towards the different properties that nanofibrous scaffolds can have (like density, fiber diameter, conductivity, mechanical properties, wettability, and alignment of fibers). The objective of reviewing the literature is to

summarize some of the effects of nanofibers on cells in one paper. The Google Scholar and Scopus websites were used to find relevant papers. For identifying the papers, several keywords and search terms were used, e.g., cell behavior, migration, viability, adhesion, growth, proliferation, and differentiation, nanofiber diameter, porosity, density, conductivity, stiffness, mechanical properties, alignment, wettability, etc. The variables and outcomes extracted from each paper were nanofiber properties, cell type, and cell behavior. Journals of used papers are indexed under the ISI Web of Science database.

Results: 1- Fiber diameter Nanofiber diameter influences cell response, and this response varies depending on the cell line. In a study by Pelipenko et al. [15], PVA nanofibers with a diameter ranging from 70 to 1120 nm were fabricated, and the behavior of keratinocyts and skin fibroblasts was evaluated on the nanofibers. More so than fibroblasts, keratinocyte size, morphology, and actin organization were influenced by nanofiber thickness. Particularly, keratinocytes grown on nanofibers were smaller and more spherical than control cells, while fibroblasts were barely impacted. They spread across the growth surface and remained essentially unchanged. When keratinocytes were grown on 305 nm thick nanofibers, the cell proliferation as measured by their metabolic activity was at its highest, while fibroblasts grown on analogous nanofibers experienced decreased proliferation. Compared to keratinocytes, fibroblasts showed greater mobility. On nanofibers with a diameter of 300 nm, cell mobility was reduced in both tested cell lines [15]. For implantation and transfer of olfactory ensheathing cells (OECs), silk fibroin nanofibers with diameters of 400 and 1200 nm were prepared by Wu et al [16]. The results showed that 400 nanometer fibers resulted in more cell adhesion, growth, and migration. As shown in Fig.1, The area of cell spreading on 400 nm silk fibroin fibers was noticeably greater than that on 1200 nm silk fibroin after 4 days. At 7 days, it was found that the OECs grown on the 400 nm TSF fibers and the 1200 nm silk fibroin fibers had significantly different spreading areas. Quantitative analysis also showed that at 4 and 7 days, OECs on 400 nm TSF fibers had significantly longer maximum process length than OECs on 1200 nm fibers. Xie et al. investigated the effects of poly (L-lactic acid) (PLLA) fiber matrices on bone marrow mesenchymal stem cells' (BMSCs') cellular responses, including cell adhesion, migration, proliferation, and osteogenesis [17]. The diameters of the fiber matrices were 600 nm for the nanoscale and 1200 nm for the microscale, respectively. After 24 hours of cell culture, findings showed that nanofibers could influence cell morphology and encourage BMSC migration. Compared to microfibers, PLLA nanofibers had higher osteogenesis and higher cell growth, and cell migration speed (Fig. 2) for BMSCs. Contrary to the results of this study, another study by Badami et al. [18] showed that density of osteoprogenitor cells, cultured on

PDLLA, PLLA, PEG-PDLLA and PEG-PLLA fibers (with diameters ranging from 140 nm to 2.1 μm) increased with fiber diameter. Also, a higher aspect ratio and the extension of lamellapodia along individual fibers were seen in cells on 2.1 μm diameter fibers, which is consistent with a contact guidance phenomenon. The adhesion of osteoblast, fibroblast, chondrocyte, and smooth muscle cells on carbon fibers (with a diameter ranging from 60 to 200 nm) was investigated by Price et al., and it was found that compared to larger diameter nanofibers, only osteoblast adhesion improved in smaller diameter ones, and the adhesion of other cells was not affected by the dimensions of electrospun carbon fibers [19]. Glioblastoma cells' migration on uniaxially aligned chitosan-PCL fibers with diameters of 200 nm, 400 nm, and 1.1 μm was observed in the study of Kievit et al. [20]. By measuring the net distance, a cell traveled from its starting point and then plotting the distance against time, effective cell speed was determined. According to Fig. 3, the fastest effective cell speed was seen in nanofibers with diameters of 400 nm. This speed is comparable to that of cells invading along microvessels in vivo. The cells expressed higher levels of invasion-related genes on the aligned 400 nm fibers than they did on the 1.1 μm fibers, suggesting that the fibers' greater curvature encouraged migratory behavior. These results imply that controlling nanofiber diameter offers a promising opportunity to improve tissue scaffold design because cells can distinguish between nanofibers of various sizes and react accordingly. 2- Fibers alignment The orientation of the cells and the tension of the fibers, which are influenced by their geometrical patterns, are the phenomenon of contact guidance [18]. The cells on the nanofibers are affected by this phenomenon in terms of how they behave. In research by Mi et al., random, aligned, and orthogonally polyurethane nanofibers were synthesized that were electrically conductive with CNT and poly(acrylic acid) (PAA) [21]. Results showed that the orientation and migration of 3T3 fibroblast cells matched the orientation of the nanofibers. Randomly oriented PVA nanofibers have been shown by Pelipenko et al. to delay keratinocyte adhesion while improving their strength, significantly changing their morphology, raising their metabolic activity, and restricting their mobility [22]. They have demonstrated that the small interfiber pores prevent whole cells from efficiently penetrating the nanofibrillar network. While cell nuclei remain on the surface of the electrospun scaffold, flexible cell parts can enter the nanofibrillar network. The random orientation of nanofibers, which does not offer consistent pathways for successful cell infiltration, is another factor contributing to poor cell mobility. Consequently, nanofibrillar support with nanosized interfiber pores may be used to promote efficient cell proliferation and quicken the healing of wounds, but not for three-dimensional tissue regeneration. The researchers also demonstrated that aligned nanofibers can successfully control cell migration and proliferation, demonstrating the importance of this property of nanomaterials for the successful regeneration of

tissues with a highly organized structure [22]. In another study, random and aligned PANi nanofibers were synthesized and seeded with myoblasts [23]. It was found that Young's modulus as well as the tensile strength of aligned fibers are higher than those of random fibers because when the force is applied to the fibers, the tension resulting from the force is equally applied to all fibers. Although the arrangement of fibers did not affect cell proliferation and growth, the growth of cells on random fibers showed flat and multipolar cell morphologies, while in aligned fibers, cells had a bipolar morphology and were attached to individual fibers. According to the results, the arrangement of nanofibers had a significant effect on the growth of myotubes (Fig. 5). While in random nanofibers, only about 10–20% of myotubes were aligned with the Y axis. The length of myotubes was also dependent on the conductivity (the amount of polyaniline in the polymer) and the arrangement of the nanofibers. It was also found that the alignment improved the differentiation of myoblast cells into myotubes (Fig. 11). In an interesting study, the behavior of C12 cells on polystyrene nanofibers with different arrangements (single fiber, two parallel fibers, and crossed fibers) and on a flat surface was investigated [24]. A comparison was made of the shapes of the cells planted on a flat surface, a single fiber, two parallel fibers, and crossed fibers, which resulted in cells with flat, spindle, parallel, and polygonal shapes, respectively (Fig. 6). Then, the migration speed of cells with different shapes was measured: The polygonal cells present at the intersection of fibers had the lowest migration speed. Spindle cells are located on a fiber and tend to be stretched in its direction, and since they have two focal adhesions and can migrate only in the axis of their fiber, they are suitable for researching the effect of fiber diameter on cell adhesion and migration [24]. So, the different geometries of nanofibers affect the migration speed of cells. Due to contact guidance, cells migrate along aligned nanofibers in a linear direction that corresponds to the direction of fiber orientation, increasing the speed of migration. When 3T3 fibroblasts were cultured on thermoplastic polyurethane nanofibers, for example, the migration speed of the cells cultured on uniaxially aligned nanofibers was roughly twice that of the cells cultured on random nanofibers for a similar nanofiber diameter [21]. On mats made of electrospun PLA and PCL nanofibers, respectively, astrocytes and L929 cells were found to exhibit comparable behaviors [25], [26]. Aligned nanofibers have been shown to speed up the migration of stem cells. For a given fiber diameter, human neural progenitor cells and mesenchymal stem cells (MSCs) both demonstrated faster migration rates on uniaxially aligned nanofibers than in the case of random nanofibers [27], [28]. To study how the cytoskeleton changes during cell migration, Dai et al. devised a simple fabrication method using nanofibers with different topographies that mimicked the alignment of extracellular nanofibers [29]. For the purpose of time-lapse imaging analysis, they used a breast carcinoma cell line. They discovered that biointerface

anisotropy modified cell morphology and mediated the migration pattern. Cells on anisotropic nanofibers exhibited an extending spindle shape morphologically. The topographic pattern on the biointerface was patterned by the migration trajectories. Besides, aligned nanofibers induced a caterpillar-like model of migration (Fig. 7) through the protrusion-retraction cycle, which was indicated by periodic variation of aspect ratio and velocity of cells. The biointerface anisotropy triggered vimentin filaments and microtubule networks preferentially oriented along the alignment of nanofibers. And the velocity of cell mobility enhanced by vimentin, β-catenin or CDC42 knockdown was significantly enhanced on aligned nanofibers. Thus, they implied that biointerface anisotropy modulated the migration of breast cancer cells and was associated with the reorganization of the cytoskeleton [29]. 3- Fibers density Many studies have been conducted to construct scaffolds with larger interfibrillar porosity, or lower density, to allow our nanofibrous structure to provide a 3D environment instead of 2D itself. Compared to the usual 2D scaffolds, 3D scaffolds have more internal surface area and pore size and thus improve cell infiltration [30]. In a study by Huang et al., a platform made of electrospun nanofibers that had been carefully aligned and densely packed was created to prevent cell migration [31]. An inverse relationship between the cell migration rate and nanofiber density was observed when cells were cultured on nanofibers of various fiber densities (Fig. 8). This was attributed to the formation of focal adhesions. While focal adhesions in the dense fiber mats were large, aligned with the nanofibers, and dispersed throughout the cells, those in the sparse fiber matrix were small [31]. According to Wang et al., fibers with a large diameter were packed more tightly than those with an intermediate or small diameter [32]. They revealed a direct correlation between fiber density and cell migration, in contrast to Huang's study results. The Schwann cells migrated the most widely on the large PLA fibers and the shortest distances on the small nanofibers on uniaxially aligned PLA fibers with different diameters (large, 1325 ± 383 nm; intermediate, 759 ± 179 nm; and small, 293 ± 65 nm). The dense fibers served as barriers to stop the Schwann cells from crossing onto them. Since there was a large distance between each fiber on the intermediate and small fibers, these fibers were unable to give off enough topographical cues to direct the migration of Schwann cells. Berti et al., synthesized bacterial cellulose nanofibers with low and high densities (porous and entangled, respectively) and evaluated the viability of human umbilical vein endothelial cells (HUVECs) on them. Results showed that in a period of 20 days, more cells were viable on porous (less dense) nanofibers (Fig. 9) [33]. The high density of nanofibers may also inhibit the diffusion of growth factors in tissue engineering applications [34]. Chen et al. used PCL nanofiber scaffolds with different densities to investigate the relationship between nanofiber density and osteogenic differentiation [35]. The ability of hBMSCs to differentiate into osteoblasts was assessed after 14

days using osteogenic marker gene expression and after 50 days using calcium mineralization, demonstrating improved osteogenic differentiation with a rise in nanofiber density. Wang et al. achieved different densities of bacterial cellulose nanofiber by changing the bacterial density during the biosynthesis of cellulose [36]. According to their results, a scaffold with a higher bacterial cellulose nanofiber density may encourage the proliferation of adipose-derived stem cells (ADSCs). It's interesting to note that ADSCs seeded in scaffolds with higher bacterial cellulose nanofiber densities displayed more spherical and smaller morphology, suggesting the potential preservation of ADSC phenotype. Rnjak-Kovacina et al. synthesized low- and high-porosity synthetic human elastin scaffolds. Both types of scaffolds displayed Young's moduli comparable to those of native elastin. Primary dermal fibroblasts could attach, spread, and proliferate on scaffolds with low and high porosities, but only scaffolds with high porosities allowed for active cell infiltration and migration [37]. 4- Electrical conductivity of fibers Electrical stimulation is beneficial for tissue engineering scaffolds because it regulates cell adhesion, migration, proliferation and differentiation. It also increases DNA synthesis, collagen and protein formation for cardiac [38], [39], nerve [40], and muscle [41] regeneration and wound repair [42]. Conductivity can be improved with the help of conductive fillers (graphene, carbon nanotubes, etc.), conductive polymers (polythiophene, polypyrrole (PPy), polyaniline (PANi)) and conductive metals (silver and gold nanoparticles) [43], [44]. Electrical stimulation has a significant impact on the regeneration of tissues like nerve and myocardium because these tissues naturally transmit electrochemical signals throughout the entire tissue [45]. Therefore, it's crucial to use materials with electrical conductivity to repair these tissues' damage. It has been suggested that electrically responsive cells, such as nerve and cardiac cells, could multiply more rapidly when contained within conductive polymer nanofibers. After 8 days of cell culture, neural stem cells on PLLA/PANi scaffolds proliferated more than those on PLLA nanofibers [46]. Even with a 30% increase in the PANi component of the composite, PANi was incorporated into PLCL scaffolds to improve myoblast proliferation [47]. Similar to this, H9c2 rat embryonic heart cell proliferation was greater on 15% and 30% PANi-gelatin composite nanofibers than on either tissue culture polystyrene or gelatin scaffolds [48]. However, a high concentration of conductive polymers in nanofibers might prevent cell growth. According to studies, when the concentration of PPy was 15%, the proliferation of cardiomyocytes on PPy/PCL/gelatin nano-fibers increased, whereas when the PPy concentration was 30%, the cell proliferation was inhibited [49]. A scaffold with cellulose nanofibers modified with polythiophene and polypyrrole derivatives was fabricated by Zha et al [50]. Compared to unmodified and non-conductive nanofibers, these conductive nanofibers showed more adhesion and proliferation of PC12 nerve cells. Also, cell viability was higher

on modified conductive polymers (Fig. 10). In the research conducted by Ku et al., the effect of the conductivity of nanofibers on cell differentiation was investigated, and it was found that by increasing the percentage of PANi conductive polymer in nanofibers, cell differentiation of myoblasts increased by 1.3 to 1.6 times (Fig. 5 and 11) [23]. 5- Wettability Greater surface wettability encourages cell attachment, spreading, focal contact formation, and metabolic activity [51]–[54]. Surface wettability also influences cell behavior. It is well known that the wettability and chemical composition of a surface also have a significant impact on cell adhesion and protein adsorption onto a substrate [55]. Due to the type of chemical bonds (covalent and ionic) holding them together, high-energy surfaces typically have higher wettability. Thus, one of the most crucial prerequisite parameters associated with cell-biomaterial interfacial interactions is wettability, which is defined by the presence of chemical groups on a material's surface [56]. For example, polyurethane nanofibers with a smaller diameter showed more hydrophilicity, which is because when the fibers are thinner, more hydrophilic functional groups are exposed to the surrounding environment. It is also said that thinner fibers have smaller pores, which causes more water absorption through capillarity [57]. In addition, thicker fibers can sometimes have large voids that trap air and increase hydrophobicity [58]. Because absorption and permeation properties are crucial for maintaining cell integrity and ensuring access to blood and nutrients during cell growth and proliferation, the capacity to absorb water is a crucial parameter for tissue engineering scaffolds [59]. Since the majority of the biomolecules required for repair are hydrophilic, increased water absorption improves tissue repair while also speeding up the rate at which the scaffold degrades. According to the literature, rat-isolated hepatocytes interact with wettable membranes more effectively than they do with non-wettable ones [60]. In another study, Lee et al. [61] prepared low-density polyethylene (PE) sheets with a wettability gradient. The interaction of various cell types (Chinese hamster ovary, fibroblast, and endothelial cells) was examined using the prepared wettability gradient surfaces. It was found that the positions of the wettability gradient surface with moderate hydrophilicity had greater cell adhesion, spread, and growth than the positions with greater hydrophobicity or hydrophilia. Regardless of the cell types used, the maximum cell adhesion and growth occurred at water contact angles of about 55°. The viability of primary neurons is also influenced by wettability, with more hydrophilic surfaces producing better viability [62]. Increased wettability does not always benefit cells; for example, motor neurons' survival on etched fibers was decreased after plasma etching increased the wettability of nanofibers [63]. 6- Mechanical properties of fibers Research has shown that mechanical properties affect cell behavior. For example, osteogenesis in stem cells can be achieved by increasing the strength and stiffness of the matrix [64], while chondrogenesis is stimulated by the softness of the

substrate [65]. Tissue modulus changes both during development and in various diseases in vivo, ranging from 0.5 kPa (adipose tissue) to 20 MPa (bone). Numerous studies [66]–[70] have shown how substrate modulus controls cell motility. The nanofiber modulus can also control how cells migrate when nanofibers are used as substrates. In one study, co-axial electrospinning was used to create fibrous mats with various surface moduli [71]. Gelatin, poly(ethersulfone), poly(dimethylsiloxane), and PCL were used as the core and sheath of the composite, respectively, to modulate the fiber moduli and preserve surface chemistry. Fig. 11 depicts how quickly a single glioblastoma cell migrates across various fibrous mats. Cell migration was fastest on nanofibers with an intermediate modulus (11 μm/h for PCL nanofibers with an 8 MPa modulus), while slower migration rates were seen on nanofibers with low and high moduli (i.e., 3.5 and 6.3 μm/h for PES-PCL and PDMS-PCL, respectively, with both 30 MPa moduli). The "catch-bond formation" mechanism [72], a cellular sensing process by which larger traction forces generated by cells can be evoked to encourage their migration, is thought to be the cause of cells' sensitivity to the fiber modulus. Park et al. showed that transforming growth factor β (TGF-β) can promote mesenchymal stem cells (MSC) differentiation into either smooth muscle cells (SMCs) or chondrogenic cells. They showed that the stiffness of cell adhesion substrates modulated these differential effects. MSCs on soft substrates had less spreading, fewer stress fibers, and a lower proliferation rate than MSCs on stiff substrates. MSCs on stiff substrates had higher expression of SMC markers α-actin and calponin-1; in contrast, MSCs on soft substrates had a higher expression of the chondrogenic marker collagen-II and the adipogenic marker lipoprotein lipase (LPL) [73]. According to experimental findings, thinner nanofibers were mechanically stronger. This is because thinner nanofibers underwent greater tensile deformation during nanofiber formation, which led to the arrangement of more polymer chains along the fiber and ultimately increased its strength [74]. Most of the time, when fibers' diameters are decreased, their densities rise, which can also aid in enhancing their mechanical properties [75]. A 3D polyethylene-glycol-dimethacrylate nanofiber hydrogel matrix with tunable elasticity was created by Wingate et al., using electrospinning and photopolymerization techniques for use as a cellular substrate [76]. Similar to the in vivo elasticity of the intima basement membrane and media layer, compression testing revealed that the elastic modulus of the hydrated 3D matrices ranged from 2 to 15 kPa. Compared to MSC seeded on soft matrices (2-5 kPa), those on rigid matrices (8-15 kPa) displayed a growth in cell area. Additionally, the elasticity of the matrix helped the cells express various phenotypes that are unique to the vascular system with high differentiation efficiency. Within 24 hours, approximately 95% of MSC seeded on matrices with an elasticity of 3 kPa demonstrated Flk-1 endothelial markers, whereas only 20% of MSC seeded on matrices with an

elasticity >8 kPa did so. On the other hand, less than ~10% of MSC seeded on matrices with elasticity 5 kPa showed a-actin markers within 24 hours, compared to ~80% of MSC seeded on matrices with elasticity >8 kPa. A potent tool for vascular tissue regeneration could be the ability to control MSC differentiation into endothelial or smooth muscle-like cells solely based on the local elasticity of the substrate. On the behavior of embryonic mesenchymal progenitor cells, Nam et al. specifically looked at how stiff the scaffolding is [77]. Core-shell electrospinning was used to create mechanically distinct scaffolds with identical microstructures and surface chemistry. Core-shell PES-PCL fibers had a modulus of 30.6 MPa, which was more than four times greater than the modulus of pure PCL (7.1 MPa). The results of the differentiation of progenitor cells into chondrogenic and osteogenic tissues on each scaffold show that the lower modulus PCL fibers offered more favorable microenvironments for chondrogenesis, as shown by a notable up-regulation of chondrocytic Sox9, collagen type II, and aggrecan gene expression as well as chondrocyte-specific extracellular matrix glycosaminoglycan production. By encouraging the expression of the osteogenic Runx2, alkaline phosphatase, and osteocalcin genes as well as alkaline phosphatase activity, the stiffer core-shell PES-PCL fibers supported enhanced osteogenesis. The results show that stem cell differentiation may be significantly regulated by the microstructural stiffness or modules of a scaffold and the pliability of each of the fibers.

Conclusion: As the potential range of tissue engineering continues to grow, the appropriate scaffolding choice is necessary to create tightly defined artificial microenvironments for each target organ. Due to their ability to mimic extracellular matrix and their tailorable properties, nanofibers are one of the most commonly used materials for tissue engineering applications. These tailorable morphological, physical, and mechanical properties have different effects on the behavior of different cell lines. Thus, to fabricate the proper scaffold for each tissue target, it is essential to understand the behavior of cells towards them. With regard to the application of nanofibers in the body, an optimal and synergistic relationship between nanofiber characteristics should be discovered because cellular behavior does not always have a direct relationship with each physical, mechanical, or morphological property of nanofibers.

Keywords: nanofibers, scaffold, cell behavior, cell response

effects of platelets on cancer progression (Review)

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Introduction: Oxidative stress (OS) is a chemical mismatch between an oxidant and an antioxidant that causes damage to redox and control or causes molecular damage. Imbalanced oxidative metabolism can produce a variety of reactive species (ROS). These ROS can cause severe changes in platelet metabolism and affect platelet function. It also leads to increased platelet procoagulant phenotype and cell apoptosis, which increases the risk of thrombosis. The generation of ROS and the subsequent activation, adhesion and recruitment of platelets are further encouraged in an auto-reinforcing loop by platelet-generated ROS. Meanwhile, cancer cells produce a higher concentration of ROS due to their fast metabolism and high proliferation rate. However, excessive ROS can lead to damage and modification of cellular macromolecules. Cancer formation and progression are strongly related to oxidative stress and oxidative damage. In addition, platelets are an important part of the tumor microenvironment and there is a significant interaction between platelets and cancer cells.

Methods: Cancer cells change platelet activation status, RNA spectrum, proteome and other properties. Excess ROS can damage cellular lipids, proteins, or DNA, altering their normal function and triggering inflammatory responses. In 1865, the association between platelets and cancer was named Trousseau syndrome. Drug studies have shown that aspirin, clopidogrel, and ticagrelor all inhibit platelets, but while they inhibit platelets, many platelet functions are also impaired. The interaction between tumor cells and platelets leads to platelet activation, which causes the release of factors that lead to tumor cell survival and proliferation.

Results: Drug studies have shown that aspirin, clopidogrel, and ticagrelor all inhibit platelets, but while they inhibit platelets, many platelet functions are also impaired. The interaction between tumor cells and platelets leads to platelet activation, which causes the release of factors that lead to tumor cell survival and proliferation.

Conclusion: Progression has been widely studied, and they not only promote the metastasis of tumor cells, but also have an inhibitory effect. Therefore, in-depth research and summary of the molecular mechanism of platelets in tumor cell metastasis is of great importance for the screening and treatment of cancer patients.

Keywords: Cancer , Tumor ,Stress , Platelets ,ROS

Efficient and Affordable Genome Editing Protocol for Concurrent Caspase 8 Associated Protein 2 Gene Knock-in/Out in Chinese Hamster Ovary Cells using CRISPR-Cas9 System and All-in-One Technology (Research Paper)

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Introduction: Hosting more than one-third of biopharmaceuticals makes Chinese Hamster Ovary (CHO) cells an attractive target for genome editing technologies to produce cell lines with high yields of recombinant protein production. Modifying genes involved in apoptosis, specifically those related to initiation of apoptosis such as Caspases 8 Associated Protein 2 (CASP8AP2), may have a positive impact on the productivity of CHO cells. Innovation and the joining of various robust strategies to the CRISPR-Cas9 system pave the way for using this technology in CHO cell engineering. Objectives: The aim of this study is to introduce an efficient and time/cost-effective protocol using homology-independent targeted integration (HITI) strategy to perform simultaneous knock in/out in a CASP8AP2 gene of the CHO cell and assess the effect of this silencing on the CHO cell productivity.

Methods: We introduce an efficient protocol for CHO cell engineering using CRISPR/Cas9 system joined HITI strategy. Using a manual selection system eases and speeds up single-cell cloning. Limitation in designing efficient gRNAs in gene coding frame, we targeted a 3' UTR of CASP8AP2 gene. In the following, the effect of this gene silencing on the expression of JRed protein in comparison with native CHO cells was investigated using flowcytometry.

Results: findings of this study displayed that CRISPR-Cas9 system joined HITI strategy provides a robust editing approach. The efficacy of this method was confirmed by achieving high efficiency of 60% knock-out clones. However, some of these clones were heterozygote, but most of them were

homozygote. No need for any complex instruments except a fluorescent inverted microscope makes this protocol possible in a laboratory with low financial and instrumental resources. In addition, the flowcytometric analysis of protein expression revealed a 2.3-fold increase in JRed expression in CASP8AP2 silenced CHO cells compared to native cells.

Conclusion: We establish a straightforward procedure for gene modification in CHO cells which resulted in the generation of knockout CHO cells with higher productivity compared to native ones. Targeted integration of the interested gene expression cassettes in a site-specific manner as well as the possibility of labelling the knock-out cells for animal studies are the proses of this strategy.

Keywords: Chinese Hamster Ovary cells, CRISPR-Associated Protein 9, CASP8AP2,3' UTR

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Efficient site-specific integration of the GFP reporter gene employing linearized dsDNA CRISPR-Cas9 method, RNP approach, and a nano-delivery system in CHO cells (Research Paper)

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Introduction: The Chinese hamster ovary (CHO) cells are widely regarded as the ideal host system for the production of recombinant therapeutic proteins primarily because of their glycosylation pattern, which is similar to that of humans. The CHO cell line development (CLD) with high protein yields is among the industry's most challenging problems. For many years, the random integration approach was employed regularly for this purpose, however, because of the heterogenicity that results from no control over the integration sites, the productivity of the chosen clones gradually decreases over time. In contrast, targeted integration (TI) techniques produce the best outcomes when choosing clones with high transgene expression levels. In these methods, the transcriptionally active genomic regions are used for integration resulting in high and stable expression. Utilizing the CRISPR-Cas9 technology has revolutionized genome manipulation due to its wide range of applications including TI by inducing double-strand break (DSB). The mammalian cells repair the DSB through different pathways mostly the error-prone non-homologous end-joining (NHEJ) and precise homology-directed repair (HDR)-related genome editing processes. In the context of a repair, if any templates are provided, under certain conditions, the cell can integrate the donor template via the knock-in process. However, most mammalian cells favor NHEJ over the HDR pathway, CRISPR-mediated integration occurs at a rate of less than 10%, while significant attempts have been made to improve it. There are several approaches for increasing the efficiency of precise integration including donor design strategies. it has recently been

demonstrated that utilizing the linearized double-strand donor could significantly increase HDR efficiency in mammalian cells. Additionally, several studies have shown that employing the Cas9/gRNA complex as ribonucleoproteins (RNPs) leads to a significant decrease in off-target effects in addition to an enhancement in TI efficiency. On the other hand, concerning using the other well-known delivery approaches such as electroporation and commercial reagents (lipofectamine, CRISPRMAX, etc.), implementing some nano polymers may be an appropriate choice for RNP delivery because of their very low cytotoxicity together with high delivery efficiency.

Methods: An in vitro RNP complex was made using the purified Cas9 protein and the sgRNA which was designed to target a specific hotspot on the CHO-K1 cell line genome. Characterized nanoparticles were combined with RNP complexes as a delivery strategy. To produce linearized donors by PCR using necessary primers, a plasmid donor including GFP and puromycin expression cassettes flanked by 1 kb left and right arms corresponding to the Chr6 hotspot site was used as the template. CHO-K1 cells were cultured under standard conditions seeded into the 24-well plate and then transfected with a nanoparticle/RNP mixture. Forty-eight hours post-transfection the cells were transferred into a 6-well plate and then incubated overnight. cells were then given the proper antibiotic concentration every two days for almost 14 days to establish a stable cell pool. To verify the presence of cells with the precise integration, 5′/3′ junction PCRs were performed to amplify the 5′ and 3′ junctions of the targeted locus and integrated transgene. limiting dilution processes were followed to achieve knock-in efficiency using individual clones. A two-sided Fisher's exact test was used to establish the statistical significance of the efficiency, which was reported as a percentage of 5′/3′ junction PCR-positive clones. Data with $p<0.05$ were considered significant.

Results: The stable cell pool was obtained and verified by 5′/3′ junction PCRs; The desired bands of approximately 1.4 kb and 1.5 kb were visualized on 1% agarose gel for 5′ and 3′ junction PCRs, respectively. Following clonal selection, the efficiency of transgene integration by the 5′/3′ junction PCR analysis of single-cell clones was evaluated through cell lysate procedures. the knock-in rate was high and approximately 51% of the recovered clones showed on-target integration (18 clones out of 35).

Conclusion: According to the results of the current experiment, the use of the in vitro linearized dsDNA CRISPR-Cas9 approach in conjunction with the RNP modality and the novel, extremely low toxic nano-based delivery vehicle significantly boosted HDR efficiency by up to 51%, making it comparable to the widely used commercial reagents.

Keywords: CRISPR/Cas9, RNP, targeted knock-in, nano-delivery, CHO

Egg freezing to preserve fertility (Review)

Arefeh Gholamhosseini,[1,*]

1.

Introduction: Usually, during a successful in vitro fertilization (IVF), several embryos are produced, and couples prefer to freeze the surplus embryos for future use. In assisted reproductive techniques such as IVF and microinjection (ICSI), embryo freezing is one of the new ways to preserve women's fertility. Social changes have led to the postponement of the age of first pregnancy. The decrease in pregnancy in industrialized countries has led to optimization of fertilization in pregnancy centers. Freezing is a promising method for storing all stages of human embryos, and this method is used to postpone embryo transfer in patients who are at risk of ovarian hyperstimulation syndrome (OHSS) or patients who are ready for radiation therapy. It is also very effective in the egg donation program. Freezing prevents the loss of extra embryos. Evidence shows that embryos that have already been frozen have better perinatal results than fresh embryos. Progesterone level is a good biomarker in this case.

Methods: In the frozen embryo transfer (FET) strategy, the desired embryos are transferred to a stimulated cycle and the remaining embryos are frozen for future use. There is a newer strategy called "freezing all" in which all embryos are frozen for future transfer in subsequent cycles as long as the uterine environment is favorable. The most common reasons for using this method are to avoid OHSS, as well as to reduce maternal blood pressure disorders, the risk of miscarriage and multiple births It should be noted that this method is not offered in women who have recovered less than 15 eggs in the stimulation cycle. In this method, PGD (Preimplantation Genetic Diagnosis) and PGS (Preimplantation Genetic Screening) are used. PGD and PGS tests are performed through IVF before embryo implantation. In this technology, genetic tests are performed on embryo cells in order to select the best embryo for implantation and continued pregnancy. When one of the parents or both of them has a known genetic disorder, PGD method is used to identify embryos with genetic disorder and thereby prevent the transfer of defective genes to the baby. On the other hand, the PGS (Preimplantation Genetic Screening) method is used to investigate aneuploidy cases in embryos resulting from laboratory fertilization.

Results: Among the egg freezing techniques, we can mention "slow freezing", in this type of freezing, it is a method of programmed step-by-step

reduction of temperature and it is long-term, this is a precise but expensive tool, and it is possible that ice crystals inside the cell that We have frozen them, which has harmful effects. Another technique is "glass freezing". In this method, we freeze the sample like glass, providing the possibility of cooling and heating with much less freezing damage than the slow freezing method. It has a high survival rate. In glass freezing, the formation of intracellular and extracellular ice is prevented. It has a lower cost and is efficient in terms of time. This type of freezing makes IVF more efficient. The biggest concern of this method is the toxicity and dangerousness of the process, and high concentrations of antifreeze cannot be used. Freezing causes extensive damage to the cell membrane, which changes the functional and metabolic state of the cell. which affects DNA fragmentation, sister chromatid exchange (SCE) and aneuploidy in the egg.

Conclusion: Freezing stress, including osmotic shock, changes in temperature, pH, and freezing toxicity may cause epigenetic and transcriptomic changes. Currently, it is not clear whether these changes affect the health of future children or not. Freezing with changes in DNA methylation level affects the normal expression of genes and gene regulatory region and depends on factors such as temperature, concentration and type of CPA (Cryoprote agents). During freezing, CPA creates an osmotic gradient that moves water from the inside to the outside while maintaining the membrane and structure inside the cell. CPAs are of two categories, 1- permeating agents: they pass through the membrane and are compounds with low molecular weight and protect the cell against damage caused by cold, such as glycerol, butanol-ethylene glycol and methyl sulfoxide. Other category 2-Non-penetrating agents: They are non-diffusible and have a higher molecular weight, such as serum proteins, sugars and polymers.

Keywords: IVF Glass freezing Slow freezing Frozen embryo transfer (FET) Cryoprote agents (CPA)

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Emergence of Gram-Negative Bacterial Infections during COVID-19 Pandemic in Sari Cardiology Hospital (Research Paper)

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Introduction: The COVID-19 pandemic caused by the coronavirus SARS-CoV-2 has resulted in a global health crisis with respiratory complications being the primary cause of mortality. Evidence suggests an increase in secondary bacterial infections or hospital-acquired infections, particularly caused by mostly gram-negative bacteria. These bacteria pose a great threat to patients due to their resistance to most antibiotics which makes them difficult to treat. Prolonged hospital stays and the use of medical devices increase the risk of acquiring these infections. This paper provides an in-depth review and statistics of gram-negative bacterial infections during COVID-19 pandemic in Sari Cardiology Hospital.

Methods: This study analyzed data from patients admitted to the hospital between July 2020 and February 2022. We collected demographic information, medical histories and laboratory results. 351 gram-negative samples were isolated from patients. Microbiological cultures were performed on respiratory samples, blood cultures, stool and urine samples and other relevant specimens from patients with signs of infection. Gram-negative bacteria were identified using standard laboratory techniques such as antibiotic susceptibility test, TSI, IMViC and other methods. Disk diffusion testing was performed according to CLSI standards.

Results: A total of 351 patients were diagnosed with gram-negative bacterial infections. The most frequently isolated gram-negative bacteria was

Escherichia Coli, accounting for 60.3% of all cases. Some other gram negative bacteria collected were Klebsiella, Pseudomonas, Citrobacter, Acinetobacter, Enterobacteriacae and CoNS. Antimicrobial susceptibility testing revealed varying resistance patterns among the isolated gram-negative bacteria e.g. 54% of the identified E.Coli strains showed resistance to commonly used antibiotics, such as ciprofloxacin. Or 68% of Enterobacteriacae strains showed resistance to carbapenem.

Conclusion: This study highlights the emergence of gram-negative bacterial infections during the COVID-19 pandemic in a local hospital. Health professionals can reduce the impact of these infections by recognizing the risk factors, understanding the basic mechanisms, and adopting appropriate strategies and diagnostic approaches. Continued research and collaboration are essential for addressing this emerging concern and informing future strategies.

Keywords: COVID-19 Pandemic, Gram Negative Bacterial Infections, Bacterial Sensitivity Tests

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Emerging diagnostic and prognostic biomarkers for colorectal cancer (Review)

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Introduction: Colorectal cancer is one of the leading causes of death, being the third most frequently diagnosed cancer worldwide. Despite advances in detection and management through surgery, chemotherapy, and immunotherapy. Precisely diagnosing colorectal cancer at early stages is critical to increasing both the chances of determining the most effective treatment method and the patient's survival. The identification and validation of effective biomarkers for colorectal cancer could lead to improved screening, diagnosis, and treatment outcomes for patients. Nevertheless, the current biomarkers have some challenges. Finding a biomarker or a panel of biomarkers that have the desirable specificity and sensitivity remains an unanswered question. In this review, we will discuss emerging diagnostic and prognostic biomarkers for colorectal cancer.

Methods: To conduct this research, we studied several articles regarding "colorectal cancer biomarkers" on PubMed, ResearchGate, and several other publishers' websites.

Results: Conventional biomarkers, such as carcinoembryonic antigen (CEA) which is a protein and is sampled from stool showed 43% sensitivity and 87% specificity, or CRMP-2 has 61% sensitivity and 65% specificity, have limitations in terms of sensitivity and specificity but emerging biomarkers, including long non-coding RNAs (lncRNAs), microRNAs and circulating tumor cells, show promise in improving early detection and prognosis. For example, 91H which is a lncRNA, is associated with proliferation, migration, and invasion of the tumor. DANCR, another lncRNA, has been in relation to tumor progression and metastasis. Also, many miRNAs show dysregulation in CRC patients. For instance, miR-30a whose target gene is metadherin, miR-744

whose target gene is Notch1, miR-383 whose target gene is PAX6, and miR-1271 whose target gene is Capn4, are all downregulated in CRC cases. These miRNAs inhibit cell migration, cell proliferation, and invasion. In a study, a panel of three lncRNA including 91H, PVT-1, and MEG3 was used to test their detection performance. The results were 82.80% for sensitivity and 78.60% for specificity. In another paper, a 2-lncRNA panel including ATB and CCAT1 was used to result in 82.00% sensitivity and 75.00% specificity. For mRNA, in a study, a panel of expression of several mRNAs containing CEA, EpCAM, CK19, MUC1, EGFR, and C-Met genes was used with 87.00% sensitivity and 85.00% specificity. In another study, two mRNAs comprising TSPAN8 and LGALS4 genes exhibited 92.50% sensitivity and 67.2% specificity. These results show that in terms of functionality, we can get good answers from several other novel biomarker types.

Conclusion: Although these novel biomarkers might not show a hopeful result when used alone, when a panel of several biomarkers is used, they can cover others' weaknesses and add on their strength to come up with a desired outcome. Evaluation of these biomarkers might require more research and clinical trials to validate their clinical utility. Expanding our understanding of this field promises the discovery of high-performance and affordable biomarkers to use on patients with colorectal cancer. The focus of our study is on potential biomarkers that can be used as a diagnostic and/or prognostic tool for CRC patients.

Keywords: colorectal cancer, diagnosis, biomarker, microRNA, lncRNA

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Employing Bioinformatics Analysis to Explore Key Genes and Pathways in Prostate Cancer (Review)

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Introduction: The importance of effective prostate cancer treatment cannot be underestimated; it is vital to preserving the quality of life for those affected by this common form of cancer. Identifying new treatments through modern sciences such as bioinformatics is essential, allowing for personalized care plans tailored to the individual's needs. Additionally, these advances can help to develop preventative measures that can ultimately reduce the risk of developing this type of cancer.

Methods: From NCBI-GEO, we downloaded the Gene expression dataset GSE55945 and proceeded to analyze its Differentially Expressed Genes (DEGs), relevant Gene Ontology (GO) information, and both the Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment pathways and protein-protein interaction (PPI) networks. After this process, 135 DEGs were identified, and their results were subjected to Functional enrichment analysis, KEGG findings, and PPI network assessment.

Results: In total, 7 hub or key genes, including CAV1, MYLK, CACNA1D, CALM1, NOX4, CCK, and AOX1, were identified. Analyzes related to molecular processes showed that most genes with differential expression are involved in the "mechanism of drug metabolism". Also, the results showed that the molecular function of most genes is related to "G-protein dependent", and "inositol phosphate metabolism" processes.

Conclusion: The DEGS, Key genes, and signaling pathways identified in this study may help understand prostate cancer's molecular mechanisms and provide possible targets for diagnosing and treating this disease.

Keywords: prostate cancer; bioinformatics analysis; biomarkers; DEGS

Empowering Oral Delivery of Peptides/Proteins: The Nanoparticle Revolution (Review)

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1.

Introduction: Protein polypeptides may be chemically altered to increase membrane permeability, decrease immunogenicity, decrease bioactivity, and boost absorption via the small intestine. It enhances drug absorption and GI toxicity but shows limited protein specificity. The mucosal adhesion system may increase bioavailability and prolong protein and polypeptide medicine retention, but it is unable to increase oral permeability or stop small intestine mucosa cleansing. This article aims to offer an overview of Nanoparticle-based delivery platforms for the enhanced oral delivery of peptides/proteins.

Methods: A literature search was conducted on Scopus, PubMed, and Web of Science up to August 2023 for this purpose. We performed a title/abstract/keywords search for "Oral delivery," " biopharmaceuticals," " proteins," “peptides," “nanoparticles” and “cells”.

Results: The findings showed that the most studied oral administration method uses NPs. Because of their complexity, NPs need expensive preparation and challenging expansion. The perfect combination of ingredients has not been found because of loading capacity, loading style, and drug physicochemical properties. One of the hottest topics in TPP drug delivery technology has been oral administration as the optimal method of delivery. Given that several protein polypeptide types exist, there is no one optimum oral delivery method. . For clinical use, it is anticipated to develop an oral delivery system for polypeptides and proteins. Protein medications are protected from GI tract digestive enzymes by the stable structure of NPs. Additionally, NPs have the ability to gradually modulate drug release, which may increase the duration of an impact. But there are still issues. First, oral protein NPs have a low bioavailability. Second, the evaluation of oral therapeutic protein NPs was limited to rabbits and mice, and the results were not applicable to people. High-dose protein NPs may have long-term advantages, but they can cause the GI environment and GI epithelial cells to undergo mitosis.

Conclusion: The information is finally completely incorporated and put to use after the GI tract's mechanism, the absorption barrier, and the process of

protein polypeptide absorption are understood. Huge computers will plan the release and absorption of medications in various locations based on NPs.

Keywords: Oral delivery, biopharmaceuticals, proteins, peptides, nanoparticles, cells

Endogenous Biomarkers Analysis and False-Negative Results for SARSCov2 Using two Commercial RT-PCR Diagnostic Kits (Research Paper)

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Introduction: Real-time PCR is a commonly employed method for identifying SARS-CoV-2, the virus accountable for COVID-19. However, it is possible to encounter inaccurate negative outcomes despite the inclusion of internal controls. This research aimed to explore how utilizing different internal control substances affects the precision of SARS-CoV-2 detection kits.

Methods: During the period spanning December 2021 to January 2022, a total of 162 respiratory tract samples were gathered from individuals exhibiting symptoms suggestive of COVID-19 at Ghaem Hospital in Mashhad, IR Iran. These samples underwent an initial screening utilizing the Pishtaz Teb kit, featuring a DNA-based internal control. Subsequently, those samples yielding negative results were subjected to a secondary examination using the Geneova kit, which incorporates an RNA-based internal control. Throughout this process, both positive and negative controls were consistently employed to ensure the accuracy and reliability of the outcomes.

Results: Following the retesting using the Geneova kit, only one patient among the 162 negative samples tested positive for SARS-CoV-2. Both the Pishtaz Teb and Geneova controls consistently yielded the anticipated results. However, it's worth noting that the Geneova internal control aligned with the Pishtaz Teb control in only 44% of instances. This discrepancy may be attributed to a higher threshold cycle value for the Geneova internal control, implying potential RNA degradation during the course of the experiment.

Conclusion: Effective quality control procedures, which encompass the utilization of suitable internal control materials, play a pivotal role in ensuring precise SARS-CoV-2 detection. This study underscores the significance of opting for dependable diagnostic kits characterized by exceptional sensitivity and specificity, as this choice can substantially mitigate the occurrence of false-negative outcomes, especially in scenarios involving a limited viral presence or the early phases of the disease. The incorporation of an RNA internal control serves the purpose of detecting RNA degradation, thereby aiding in the identification of potential false-negative diagnoses. This, in turn,

contributes to enhanced disease control and management. Further research is needed to enhance the accuracy of COVID-19 diagnostic tests.

Keywords: COVID-19, Real-time PCR, internal control, false-negative diagnoses, respiratory tract samples

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Enhanced survival and accelerated perfusion of skin flap to recipient site following administration of human amniotic membrane in rat models (Research Paper)

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Introduction: The human amniotic membrane contains the cellular parts obligatory for cell integration and tissue remodeling and has high tensile strength and persistence. We theorized that such material could function as a scaffold to improve the survival of ischemic tissue in random skin flaps.

Methods: Male Albino Wistar rats (n = 30) were randomly assigned to three groups, each receiving a different model of AM on dorsal paravertebral areas: saline, amniotic membrane sheet, and micronized amniotic membrane. Digital photographs were taken, and the survival area was examined after one week. Histological analysis of skin flap tissue was performed, and the expression rate of vascular endothelial growth factor and apoptotic protein was examined.

Results: The survival percentage increased over time in all groups; however, one week after the implanted AM was increased survival in both experimental groups, with significantly greater than in the group control. In the experimental groups, there was a more regular arrangement of collagen and improved epithelialization in the flap tissue, also an increased number of inflammatory cells was observed in the control group. Additionally, VEGF and apoptotic protein expression, respectively, were significantly lower and greater in the control group than in the experimental groups.

Conclusion: These results show that a micronized membrane is an excellent scaffold for promoting flap survival

Keywords: Amnion; Collagen; Control groups; Epidermis; Humans; Male; Microvascular density; Rats; Skin;

Enhancing Apoptosis Resistance in Chinese Hamster Ovary (CHO) Cells through CRISPR/Cas9-Mediated Caspase 8 Associated Protein 2 Gene Editing (Research Paper)

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Introduction: Chinese Hamster Ovary (CHO) cells are of great interest for the production of biological drugs on a commercial scale. They are able to produce high levels of recombinant proteins, which are an important part of protein therapy and protein engineering. New genome editing technologies, such as CRISPR/Cas9, offer the potential to enhance CHO cell lines by modifying genes involved in apoptosis, the process of programmed cell death. This is because apoptosis is a major factor that limits the production of recombinant proteins in CHO cells. Objective This study aimed to investigate the role of the Caspase 8 Associated Protein 2 gene (CASP8AP2) gene in the apoptosis pathway. The CASP8AP2 gene is involved in the induction of apoptosis, and its knockout by the CRISPR/Cas9 system could lead to cells with increased resistance to apoptosis. This would allow for the production of higher levels of recombinant proteins in CHO cells.

Methods: We have developed a protocol for engineering CHO cells using the CRISPR/Cas9 system in conjunction with the homology-independent targeted integration (HITI) strategy, in which CHO cells constantly express GFP, thereby facilitating clone selection by deleting the CASP8AP2 gene. Apoptosis was assessed using flow cytometry to evaluate the effect of CASP8AP2 gene silencing on the viability of engineered cells, and the number of cells that underwent early apoptosis, late apoptosis, and necrosis compared to parental CHO cells.

Results: Our study shows that the CASP8AP2 gene, which plays a role in stimulating extrinsic apoptosis, its deletion by the CRISPR-Cas system causes resistance to apoptosis in cells lacking CASP8AP2, which shows that

this approach has a significant potential to improve the performance of CHO cells. While some clones showed heterozygosity, more than 60% of the knockout clones were successfully homozygous. This protocol does not require very complicated equipment only relies on an inverted fluorescent microscope, and allows implementation in laboratories with limited financial resources and instruments. Flow cytometry analysis showed that the deletion of the CASP8AP2 gene causes cells to become resistant to apoptosis. It can be of great help in the production of therapeutic proteins and the expression of recombinant proteins in CHO cells in the future.

Conclusion: The developed protocol provides an efficient and cost-effective tool for simultaneous knock-in/knockout of CASP8AP2 gene in CHO cells. Successful gene editing in apoptosis resistance subsequently increases protein expression, underscoring the potential for better biopharmaceutical production. These findings contribute to the advancement of CHO cell engineering and its applications in optimizing the yield of recombinant protein.

Keywords: CHO cells, CRISPR-Associated Protein 9, Homology-independent targeted integration , GFP

Enhancing Bladder Cancer Treatment: The Power of Combined Therapies (Review)

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Introduction: Bladder cancer, ranking among the most prevalent and aggressive urinary malignancies, presents significant therapeutic challenges. Although current standard treatments, which include surgery, chemotherapy, radiation therapy, and immunotherapy, have been pivotal in managing the disease, they often exhibit variable response rates, coupled with potential adverse effects. Given the complex landscape of bladder cancer therapy and the persistent limitations of monotherapeutic approaches, there is a pressing need to explore and understand innovative combination therapies. This review delves into the potential of evolving realm of synergistic approaches in bladder cancer therapy.

Methods: To assemble the information presented in this review, a thorough search was conducted on reputable databases including PubMed, Google Scholar, and ScienceDirect. The primary focus was on identifying articles pertaining to combination therapies for bladder cancer, encompassing radiation therapy, immunotherapy, chemotherapy, and targeted therapy. Searches were refined to include recent publications and prioritize those with open-access full-text availability. A meticulous examination of relevant studies enabled the extraction of pertinent information for integration into this overview.

Results: The exploration uncovers a spectrum of synergistic approaches aimed at redefining bladder cancer treatment. By fusing radiation therapy with the immune-enhancing effects of immunotherapy and the cytotoxic potential of chemotherapy, researchers orchestrate a multifaceted assault on bladder cancer cells. Preclinical studies and early-phase clinical trials underscore the promise of this approach. The convergence of chemotherapy's cytotoxic

action and immunotherapy's immune-activating properties offers a dual-pronged strategy for therapeutic amplification. However, the challenge lies in optimizing the sequence, dosing, and managing potential toxicities of these dual therapies. Moreover, strategic pairing of targeted therapies, such as FGFR inhibitors, with immunotherapy addresses the molecular heterogeneity of bladder cancer, capitalizing on specific genetic alterations prevalent in bladder cancer, such as FGFR3 mutations. While promising, tackling resistance mechanisms remains paramount for achieving optimal efficacy.

Conclusion: The burgeoning potential of combination therapies for bladder cancer treatment, backed by robust preclinical and clinical evidence, stands as a pivotal advancement in the field. As the therapeutic landscape continues to transform, precision medicine's role in guiding combination strategies is pivotal. The synergy of multifaceted interventions holds immense promise in expanding treatment horizons for bladder cancer.

Keywords: Bladder cancer, combination therapy, immunotherapy, targeted therapy, precision medicine.

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Enhancing Photodynamic Inactivation Efficacy Against Acinetobacter baumannii Using an Efflux Pump Inhibitor (Research Paper)

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Introduction: Acinetobacter baumannii is a Gram-negative pathogen which is resistant to multiple drugs (MDR) and often causes hospital-acquired infections, particularly in intensive care units (ICUs) and in patients with compromised immune systems. Infections caused by A. baumannii include pneumonia, meningitis, bloodstream infections, and surgical site infections. One effective approach to combat antibiotic-resistant pathogens is photodynamic inactivation. In this method, a non-toxic dye called a photosensitizer is exposed to low-intensity visible light or laser which generates cytotoxic reactive oxygen species or free radicals. During photodynamic inactivation, some of the photosensitizers are pumped out of the cell by efflux pumps, reducing the antimicrobial effect of the process. The objective of this study was to enhance the efficacy of antibiotic-resistant photodynamic inactivation using verapamil as an efflux pump inhibitor

Methods: Erythrosine B was used as the photosensitizing agent. The light source utilized was a 530 nm diode laser with a maximum output power of 25 mW. The bacterial suspensions were incubated with erythrosine B (50 µM) and verapamil (10 µg/ml) in the absence of light, at room temperature, for 20 minutes. Subsequently, the treated cells were exposed to the diode laser for a period of 30 minutes. Following laser exposure, the bacteria were enumerated through a tenfold serial dilution method. Controls included bacterial suspensions exposed to light alone, bacterial suspensions incubated with 0.9% sterile saline in the dark (untreated), bacterial suspensions incubated with EB (50 µM) alone or verapamil (10 µg/ml) alone, and EB (50 µM) + verapamil (10 µg/ml) in the dark.

Results: Simultaneous photodynamic inactivation using verapamil and erythrosine B dye was capable of reducing the number of live A. baumannii bacteria by more than 3 logs and inducing a lethal effect. Meanwhile, photodynamic inactivation using the dye alone reduced the bacterial count by less than 1 log and had only a sub-lethal effect.

Conclusion: The findings demonstrated that the efflux pump inhibitor verapamil led to an increase in the effective concentration of the dye in the bacterial cytoplasm and enhanced the bactericidal effect of photodynamic inactivation compared to using the photosensitizer alone.

Keywords: Acinetobacter baumannii; Photodynamic inactivation; Efflux pump inhibitor

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Enhancing the Physicochemical Properties of Polyvinyl Alcohol/Hyaluronic Acid Nanofibers for Tissue Engineering Application (Research Paper)

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Introduction: Polyvinyl alcohol (PVA) and hyaluronic acid (HA) are biocompatible and common polymers that have shown promising outcomes for electrospinning in tissue engineering. Their unique properties make them attractive materials for various biomedical applications, such as wound healing and scaffold bases in tissue regeneration, so they have been studied in many recent researches and used to develop new products in the market. However, there are some significant challenges associated with PVA and HA, such as their limited stability in biological conditions and high water solubility. Consequently, they instantly dissolve in aqueous environment and it is almost impossible to fabricate and use PVA/HA nanofibers in tissue engineering. Crosslinking is an efficient method to induce water-resistance of these polymeric fibers and it has significantly improved characteristics of electrospun nanofibers. We would optimize the crosslinking process of PVA/HA fibers in this study.

Methods: Hyaluronic acid and PVA were used and well prepared through the electrospinning method to produce nanofibers. PVA/HA nanofibers crosslinked with different methods such as methanol for 24 h, heating for 150 min at 150 ˚C, or 180 ˚C. The Water resistance of crosslinked nanofibers was evaluated by immersing them in phosphate buffer saline for 24 h. The morphology of PVA/HA nanofibers before and after crosslinking was characterized through scanning electron microscopy (SEM). Also, Fourier transform infrared (FTIR) spectroscopy was used for determining the molecular interaction of the polymers before and after electrospinning and crosslinking. The tensile test was used to characterize the mechanical strength of the electrospun mat before and after crosslinking

Results: It has been observed that the methanol crosslinked fibers dissolved at once in the aqueous medium. On the other, both of the heat crosslinked nanofibers didn't dissolve in PBS and were completely stable for at least 24 h. It was observed that when the nanofibers were heated to 180°C, their appearance changed to a brown color, and they adhered to all types of surfaces beneath them during the crosslinking process. However, subjecting the nanofibers to dry heat at 150°C did not alter their macroscopic appearance. SEM analysis revealed that the electrospun nanofibers were consistently homogenous and with an average of 203 ± 23 nm in size. Furthermore, a statistical comparison between the crosslinked and non-crosslinked mats indicated a significant decrease in nanofiber diameter following the crosslinking process. FTIR results have shown that crosslinking decreased the free hydroxyl content of the polymers which was reflected by a reduction in the hydroxyl peak intensity. The mechanical properties of the nanofibrous mats were found to be suitable for various tissue engineering applications, and no significant reduction in mechanical properties was observed following the crosslinking process.

Conclusion: This optimized dry heat crosslinking method is anticipated to enhance the physicochemical characteristics of PVA/HA nanofibers and make them more suitable for applications in tissue engineering.

Keywords: Hyaluronic acid, Polyvinyl alcohol,tissue engineering, Crosslinking

Evaluate the effect of PI3K pathway regulators with melatonin on arrested human embryos development in vitro (Research Paper)

nazaninalizadeh,[1,*]

1.

Introduction: IVF is one of the methods used for assisted reproduction. blastocyst cannot be reached by a certain percentage of the resulting embryos. According to the studies, 40 to 50% of the embryos of IVF cycles cannot reach the blastocyst stage and are stopped. Embryos stop on the third to fourth day after conception Embryos stopped before implantation are divided into three groups: type 1, which is between 2 and 4 cells, type 2, which is between 4 cells and 8 cells, and the third type, which is stopped at the primary morula stage, which type 1 is in the MZT, and the second and third types. They are disturbed at the level of glycolysis and oxidative phosphorylation. And they may be disturbed in the signaling pathways. Signaling pathways can be regulated by antioxidants. Melatonin is an antioxidant that, by activating the Pi3k signaling pathway involved in development, The signaling pathway is PI3k, which is activated by placing growth receptors on it and causes the conversion of PIP2 to PIP3 and then the activation of Akt groups. Akt inhibits the gsk3 pathway and then activates the unit pathway, which is involved in cell proliferation and self-renewal. and also through its antioxidant properties, It can cause the growth of human embryos that have been stopped.

Methods: In this study, with the consent of the subjects, other 72-hour human embryos available in the Embryology Department of the Royan Research Institute Clinic, which were clinically and microscopically used, were used. The sample collection period IR.ACECR.ROYAN.REC.1402.008 started after obtaining the code of ethics This study was conducted during three main phases. The first phase is melatonin dosing and choosing the best dose. The second phase is the culture of suspended embryos in the control group and experimental groups with the appropriate concentration obtained from the first phase in order to remove these embryos from the state of suspension and culture to the blastocyst stage The third phase, the evaluation of blastocyst embryos including the expression of OCT4, NANOG, SOX2, CDKN1A, and CCNA2 genes by q-Real-time PCR technique.

Results: Under typical IVF procedures, approximately 30% of embryos arrest development, but maintain a normal morphology and cell integrity, and do not show signs of disintegration. the embryos that were arrested on day 3 did not

reach the point of forming a morula. Based on the study and the transcriptome data, there are several reasons for this event, which can be mentioned as the failure in the activation of the fetal genome, the delay in the deletion of maternal transcripts, the creation of reactive oxygen species, and aneuploidy. Until today, limited methods have been presented to deal with the stopping of the development of the embryo. Among these solutions, you can use the supplemental culture medium and the use of antioxidants, which increase the activity of mitochondria by dealing with and/or preventing damage. Oxidative stress, as well as the regulation of cellular signaling pathways, is used Melatonin caused the arrested embryos to reach the blastocyst Melatonin antioxidants with a pi3k-activating effect had a substantial impact on the development of arrested embryos. After treatment, 11/35 embryos recommenced development However, Similarly, while many (9/35, 25%) of the embryos that recommenced development, only 1 compacted, and only (6 /35 20%)made it to the blastocyst stage. We next looked at senescent and cell cycle–related genes that increased the expression of pluripotency genes significantly compared to the control group Expression of the cell cycle inhibitor CDKN1A had also not declined melatonin partially reactivated a normal developmental program in a minority of embryos and CDKNA1 cell cycle inhibitor gene had a significant decrease in expression in the treatment group compared to the control.

Conclusion: Melatonin increases conformational changes in MT2, and activation of the αi subunit leads to stimulation of PKG through guanylate cyclase. Also, it involves PKC and ErK1/2 complexes. ERK signaling regulates six basic cellular processes in response to extracellular cues. These processes include cell proliferation, cell survival, cell growth, cell metabolism, cell migration, and cell differentiation In fact, melatonin through the receptor. Mt1 activates the pi3k signaling pathway and its downstream pathway, the Erk pathway Melatonin can play a role in the development of 72-hour arrested human embryos to reach the blastocyst.

Keywords: IVF-arrested- embryo-antioxidant- melatonin

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Evaluating Health promoting Lifestyle Profile among Menopausal Women: A Meta analysis (Research Paper)

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Introduction: Menopause is one of the most drastic experiences in a woman's life because of a spectrum of vasomotor symptoms which affect the quality of life and lifestyle. Although many treatments for these symptoms are available, they can be used for only a short duration. The nonpharmacologic therapies associated with healthy lifestyle behaviors are increasing. Health-Promoting Lifestyle Profile- II (HPLP-II), a self-report questionnaire designed to assess an individual's engagement in health-promoting behaviors, has focused on six dimensions of behavioral health promotion. This study aimed to review the degree of lifestyle modification in menopausal women based on the questionnaire HPLP-II.

Methods: A comprehensive search was conducted for articles using HPLP-II after literature as the identified instrument for menopausal women's lifestyle, followed by a meta-analysis.

Results: Among 8525 unique titles, 13 studies with 2648 participants were included. Quality assessment was “good” for most of them. The summary effect of participant age was 55.78 years and 49.1 years for menopausal age. Analysis of the pooled studies yielded a mean HPLP total score of 127.69. There was no evidence of publication bias.

Conclusion: Our meta-analysis showed a moderately rated health-promoting behavioral profile in menopausal women. The spiritual growth subscale received the highest score, whereas physical activity received the lowest score and was at the lower limit of the moderate range. Health policymakers, patients, and healthcare providers can use these results to improve the healthy lifestyles of menopausal women.

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Keywords: fhgHealth promotion, Menopause, Lifestyle, HPLP-IIjhkj

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Evaluating the effect of different herbal enhancers on colonic absorption of mesalazine (Research Paper)

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Introduction: Mesalazine (5-aminosalicylic acid; mesalamine), an anti-inflammatory agent, the active derivative of sulfasalazine, which is used in the treatment of mild to moderate active ulcerative colitis and controling inflammation by inhibiting cyclooxygenase and reducing prostaglandin production in the colon. The purpose of this study is to investigate the increase in colonic absorption of mesalazine by using the different herbal enhancers.

Methods: For the purpose of the effect of absorbing herbal additive first, the intestines were placed in contact with the absorbtion of additives such as eucalyptus, menthol, olive oil and oleic acid for 4 hours, and then, the drug passed through the treated colon. The effect of additive adsorption was investigated by calculating the permeability parameters by FT-IR technique.

Results: The results indicate that the absorption of all additives used increased the permeability of mesalazine to water but, among the absorption additives, menthol with Jss = 0.0949 ± 0.0001 and permeability percentage of 97.72% had the highest absorption. The results of FT-IR of the intestine pre-contacted with menthol indicate asymmetric C-H and C-H symmetric water shifts.

Conclusion: The results indicate that various mechanisms such as lipid liquefaction, lipid degradation as well as irreversible denaturation of intracellular proteins (derived from eucalyptus oil, menthol, oleic acid and olive) have the greatest effect on increasing drug penetration.

Keywords: Mesalazine, enhancer, gastrointestinal permeability, laboratory rats

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Evaluation of anti-biofilm activity of Lactobacillus rhamnosus GG and Nisin on the expression of aap, ica-A and ica-D as biofilm-associated genes of Staphylococcus epidermidis (Research Paper)

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4.

Introduction: In the present study, the anti-biofilm activity of Lactobacillus rhamnosus GG and Nisin was investigated on biofilm-forming abilities of Staphylococcus epidermidis strains and the expression of the biofilm-associated genes.

Methods: In this study, the standard strain of L. rhamnosus GG (ATCC 53103) and Nisin were used to assess their anti-microbial and anti-biofilm effects on S. epidermidis (RP62A).

Results: The MIC and MBC analysis showed that Nisin at 256 µg/mL and 512 µg/mL, and L. rhamnosus GG at 1×107 CFU/ mL and 1×108 CFU/mL have anti-microbial activity compared to the negative control respectively. L. rhamnosus GG bacteria and Nisin inhibited the biofilm formation of S. epidermidis based on optical density of at 570 nm (P <0.001). The relative mRNA expression of aap, icaA, and icaD genes was significantly reduced compared to the negative control after treating S. epidermidis with sub-MIC of Nisin (0.44, 0.25 and 0.6 fold, respectively) (P>0.05). In addition, the relative expression of aap and icaA genes, but not icaD (P>0.05), was significantly lower than the negative control (0.62 and 0.7 fold, respectively) (P>0.05), after exposure to the sub MIC of L. rhamnosus GG.

Conclusion: Nisin and L. rhamnosus GG exhibit potent activity against biofilm-forming abilities of S. epidermidis and these agents could be utilized as an anti-biofilm agents against S. epidermidis infections.

Keywords: Staphylococcus epidermidis; Probiotic; Lactobacillus rhamnosus GG; Nisin; Biofilm

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Evaluation of antibiotic susceptibility, biofilm formation ability, prevalence of extended-spectrum beta-lactamase (ESBL), multi-drug resistant (MDR) in clinically isolates Escherichia coli and Klebsiella pneumoniae (Research Paper)

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Introduction: Escherichia coli and Klebsiella pneumoniae are opportunistic bacteria with high prevalence and antimicrobial resistance (AMR). The sensitivity pattern and biofilm formation ability and antibiotic sensitivity of biofilm-forming isolates were investigated on 104 K. pneumoniae and 100 E. coli isolates

Methods: Sample collection and identification of bacterial isolates was done. Antibiotic susceptibility testing was performed based on disc diffusion method. ESBL phenotypes were detected through the results of the antibiogram. MIC was measured using microtiter plate assay. Biofilm formation capability was accomplished. Total DNA was extracted. PCR was performed. Statistical analysis was done.

Results: Disc release sensitivity tests were performed according to Clinical Laboratory Standards Institute (CLSI) guidelines using discs containing gentamycin, amikacin, imipenem, tetracycline, ceftazidim, cefepime, ceftriaxone, cefotaxime, ciprofloxacin, and ampicilin. The highest level of resistance was against ampicilin (80% in E. coli and 96% in K. pneumoniae). 21 isolates of E. coli and 50 isolates of K. pneumoniae were able to form biofilm, which 7 isolates were able to form strong biofilm. In strong biofilm-forming isolates, the highest level of resistance was related to tetracycline (7% in E. coli and 7.2% in K. pneumoniae). 47 isolates of E. coli (47%) and 21 isolates of K. pneumoniae (20.2%) were classified as ESBL producers. 72 isolates from E. coli and 52 isolates from K. pneumoniae were classified as MDR.

Conclusion: Considering the role of biofilm in the transfer of genes, appropriate health policies and the correct administration of effective antibiotics can help in prevention.

Keywords: Eshershia coli, Klebsiella pneumoniae, Antibiotic resistant, Biofilm

Evaluation of antibiotics on treatment of dental caries and investigating their side effects (Review)

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Introduction: Dental caries, also known as "tooth decay," is one of the most common chronic and infectious illnesses of the whole oral cavity. The primary reason for losing teeth in young adults and children is dental caries, leading to tooth root deterioration in the elderly. The principal etiologic agents of dental caries are cariogenic bacteria, which can ferment carbohydrates to create acid and demineralize tooth surfaces. Lactobacillus spp, Actinomyces spp, Streptococcus mutans, and other types of bacteria not using air are estimated to be the primary causes of dental caries. This review summarized the use of any antimicrobials such as systemic antibiotics in clinical settings up to this point and also on checking for the side effects of these antibiotics.

Methods: The search engines used to find published data between the years 2000 and 2020 include well-known specifically Scopus databases, ScienceDirect, PubMed, and Google Scholar. The search technique was to download and recover distributed writing managing compelling anti-microbials for preventing dental decay. Specific keywords such as “antibacterials”, “dental caries”, “antibiotics ”, “antibiotic side effects”, “bacterial infection”, and “dental plaque “ were used. Four hundred studies were funded. Based on abstracts, 360 studies were omitted, and 40 went for full reading texts were finally included in the criteria.

Results: Antibiotics of penicillin V and penicillin G were the primary choice for treating dental infections of classic etiology. However, using penicillin can lead to some bad side effects, such as diarrhea, hypersensitivity, rash, neurotoxicity, urticaria, and nausea. The broad-spectrum antibiotic tetracyclines can make protein amalgamation more difficult by restricting to the 30S ribosomal subunit in the mRNA interpretation complex. Some of tetracycline‘s side effects include stomach cramps, sore tongue or mouth, diarrhea, headache (rarely), skin photosensitivity, and vision issues, as well as kidney damage that has also been reported. Some Side effects of

metronidazole, such as a metallic taste, nausea, skin flushing, tachycardia, headaches, shortness of breath, and loss of appetite, have been reported. By reversibly restricting to the P site on the 50S subunit of the bacterial ribosome, macrolides can inhibit ribosomal translation and obviate peptidyl transferase from attaching the tRNA-attached peptide to the next amino acid as it grows. Side effects include myopathy, long QT syndrome, cholestasis, and recycling through the enterohepatic system. Mitral annuloplasty and susceptibility-guided antibiotics containing benzylpenicillin and clindamycin have been shown to inhibit S. Lactobacillus and mutans acidophilus development in vitro. Some Side effects such as diarrhea, pseudomembranous colitis, vomiting, abdominal cramps or pain, nausea, and contact dermatitis.

Conclusion: From infancy to old age, dental caries are the most popular oral epidemic diseases. The treatment of dental caries using drugs that focus on the particular cariogenic microorganism is about as effective as systemic antibiotics. Another basic idea is that The oral cavity of the human body is in a condition of concurrence with a microbial local area. Antibiotics' effects on the community of oral microorganisms and their connection to oral cavity disease have been the subject of few studies. Maintaining ecological balance and also future direction for the creation of new oral cavity-applicable antimicrobials is essential to the treatment of oral diseases because of the strong connections between the microbiome and diseases.

Keywords: Antibiotics Treatment Dental caries Side effects

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Evaluation of anticancer effects of NL2-targeted polycationic nanoparticles containing decoy oligodeoxynucleotide against Nanog in breast cancer cell line (SKBR3) (Research Paper)

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Introduction: Aberrant expression of NANOG in cancer stem cells (CSCs) has been linked to resistance against conventional therapeutic strategies in certain types of cancer. In the present study, we explored the anticancer effects of silica nanoparticles coated with poly(l-DOPA), labeled with NL-2 peptide, and containing NANOG decoy oligodeoxynucleotides on SKBR3 breast cancer cells.

Methods: NANOG decoy oligodeoxynucleotides, designed and synthesized based on the Sox2 gene promoter, were loaded on SiO2@PDOPA-NL2 nanocomposites. The physicochemical properties of these nanocomposites were investigated using FTIR, DLS, SEM, and release tests. The NL2 peptide was used to increase the selectivity of drug delivery to HER2-positive tumor cells. Subsequently, the cellular uptake of these nanocomposites was evaluated through an uptake test, and their anticancer properties were investigated using MTT, cell cycle, apoptosis, and scratch assays on the SKBR3 cell line.

Results: The tests related to the physicochemical properties of the nanocomposite showed nanometer size, spherical shape, and correct synthesis. The release of ODNs from the nanocomposites was time-dependent, with the peak release occurring at 24 hours. The NL2-targeted nanocomposites were efficiently taken up by SKBR3 cells, targeting the HER2 receptor. The effects of nanocomposite treatment showed significant cell growth inhibition, apoptosis induction, and cell cycle arrest.

Conclusion: The results suggested that SiO2@PDOPA-DEC-NL2 can potentially suppress the proliferation of SKBR3 cells. Therefore, the presented nanocomposite system can be a promising approach for targeted drug delivery in cancer treatment.

Keywords: decoy oligodeoxynucleotides, NANOG, NL-2 peptide, silica nanoparticle, breast cancer.

Evaluation of biofilm associated genes and antibiotic susceptibility among Klebsiella pneumoniae isolates (Research Paper)

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Introduction: Klebsiella pneumoniae is an opportunistic bacterium, which is globally recognized for its high prevalence and antimicrobial resistance (AMR). Antibiotic susceptibility among MDR and non MDR and biofilm forming isolates and prevalence of biofilm associated genes were performed on 104 K. pneumoniae isolates.

Methods: Sample collection and identification of 104 bacterial isolates was done. Antibiotic susceptibility testing was performed based on disc diffusion method. ESBL phenotypes were detected through the results of the antibiogram. The MIC of ceftazidime and imipenem antibiotics was measured. Biofilm formation capability was accomplished. DNA was extracted. PCR was performed. Statistical analysis of the results was accomplished.

Results: Disc diffusion method showed that the highest susceptible was against amikacin (56.7%), imipenem (54.8%) and gentamycin (52.8%), respectively. In K. pneumoniae isolates forming a strong biofilm, the highest resistance and the highest antibiotic sensitivity are related to tetracycline (5, 7.28%) and ceftriaxone (2, 1.94%), respectively, and in the isolates forming a moderate biofilm, amikacin (15, 14.56%), ceftriaxone and imipenem (10, 9.7%) respectively, and in isolates forming weak biofilm, are respectively related to amikacin (26, 25.2%) and imipenem (18, 17.47%) and in non-biofilm-forming isolates, were related to amikacin (52, 50.4%) and ceftriaxone (30, 29.12%), respectively. In MDR K. pneumoniae isolates, the highest rate of antibiotic sensitivity and resistance was related to imipenem (16%) and amikacin and cefotaxime (49%), respectively, and in non-MDR, it was related to ceftriaxone (45%) and amikacin (49%). Among all K. pneumoniae isolates, the luxS gene has the lowest frequency. In MDR, luxS gene has the lowest frequency in isolates producing strong biofilm and non biofilm. In non-MDR, luxS gene has the lowest frequency in isolates producing moderate and weak biofilms and non biofilm.

Conclusion: Considering the undeniable role of biofilm- formation on gene transferring and bacterial high durability in the hospital environment, proper

administration of effective antibiotics and disinfection methods must be considered.

Keywords: Klebsiella pneumoniae, Drug resistance, Biofilm

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Evaluation of Casp8 and Casp9 Gene Expression in Gastric Cancer and Healthy samples (Research Paper)

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Introduction: Gastric cancer is recognized as the fourth most common cancer in the world. Several factors are involved in gastric cancer, including suppression of apoptotic initiator genes (caspase-8 and caspase-9). This study aimed to evaluate the expression of caspase 8 and 9 genes in healthy and healthy individuals.

Methods: In this study, 30 patients with gastric cancer and 30 healthy individuals from the general population were selected as the control group. After blood sampling, RNA was extracted using the yekta tajhiz azma kit and the cDNA was prepared using the Taccara kit. Expression of Casp8 and Casp9 genes was then evaluated using Real-Time RT-PCR. Data were analyzed using Rest software.

Results: According to the obtained data, statistical analysis was performed ($p < 0.05$) by Rest software, the expression of Casp8 and Casp9 in cancers was significantly decreased compared to healthy ones. ($pCasp8 = 0.0022$) and ($pCasp9 = 0.0092$). This finding indicates a decrease in the expression of this gene in gastric cancer.

Conclusion: Due to the pre-apoptotic role of Casp8 and Casp9 within the cells, it can be concluded that this gene is suppressed and the cells progressed to the tumor in gastric cancer specimens. The two genes also can be a good marker for cancer detection and prevention of the occurrence of cancer.

Keywords: Gastric Cancer, Caspase 8, Caspase 9, Real-Time RT-PCR Technique

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Evaluation of changes in blood serum lipids after lipoabdominoplasty surgery in surgical specimens in the Mehr center of Tehran city (Research Paper)

Maryam Nafisi,[1,*]

1.

Introduction: Background and purpose: Today, obesity has become a chronic and common disease that can cause a lot of harm to a person and cause serious health problems. Obesity is the cause of various diseases such as diabetes, hypertension, dyslipidemia, coronary diseases, etc. There are many treatment methods for obesity sufferers, which due to the vast changes in people's lifestyle, faster, less complicated and more effective methods have been more welcomed; Meanwhile, liposuction has been one of the most popular methods to correct obesity, especially local obesity, in recent years. Classical abdominoplasty surgery is a surgical method to improve the appearance of the abdomen by removing excess fat and skin in the hypogastric area, repairing the defect in the muscle layer of the abdominal wall with wide incisions. In this study, metabolic changes following lipoabdominoplasty were investigated.

Methods: This case-control study was conducted with the aim of investigating Chol Total, HDL, LDL, TG factors on 30 obese patients and 30 healthy individuals. After obtaining informed consent from the patients, fasting blood samples were taken 24 hours before the operation and then 4 weeks after the operation. After separating the serum samples, the changes in metabolic factors were measured using medical diagnostic kits It was analyzed by SPSS software version 22.

Results: In this study, statistical analysis was taken at the statistical level of 95%, and comparing the two groups of patients with healthy, cholesterol and LDL as bad lipids decreased significantly, HDL as good lipids increased significantly, and triglycerides No significant change range was observed. Also, comparing the two groups of patients before and after the surgery, the triglyceride level increased significantly after the operation, and the cholesterol, LDL, and HDL levels did not change significantly.

Conclusion: According to the findings and the fact that lipabdominoplasty is a surgical method to improve the appearance of the abdomen and is used as a cosmetic surgery, the change in serum fat profile after lipabdominoplasty, this

procedure can improve Fat profile and improvement of life of obese patients can be effective.

Keywords: lipoabdominoplasty-cholesterol-LDL-HDL-triglyceride-obesity

Evaluation of EGFR expression in Odontogenic lesions: A comparative study between "Amaloblastoma and Odontogenic keratocyst" (Research Paper)

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Introduction: Introduction: Ameloblastoma (AM) and odontogenic keratocyst are common odontogenic lesions that have a high rate of recurrence. Considering the determining role of epidermal growth factor receptor (EGFR) in cell proliferation and survival of epithelial cells and the controversial results of previous studies regarding the expression of this marker in odontogenic cysts, this study aimed to compare the expression of EGFR marker in AM and OKC.

Methods: Methods and Materials: In this study, 46 specimens (20 AM and 26 OKCs) were evaluated; 5-µ sections were prepared for Immunohistochemical staining using EGFR antibody. Immunohistochemical analysis was performed using super sensitive one-step polymer-HRP. The expression of EGFR was first evaluated by quantitative assessment via measuring the count of stained cells in the three stained layers in AM (ameloblastoma-like cells, Stellate reticu, and all layers) and OKC (basal layer, suprabasal and basal layers, and all layers). Next, the mean percentage of stained cells in each specimen was scored and classified

Results: Results: The mean percentage of EGFR expression was 81,39±10,41% in the AM and 78.05±19.27 in the OKC specimens. The EGFR expression was significantly no different between AM and OKC according to Mann-Whitney. However, the Mann-Whitney test showed no significant difference in the EGFR score (P=0.141). The chi-square test revealed no significant difference in EGFR expression in different layers (P=0.303).

Conclusion: Conclusion:The EGFR expression showed no significant difference between AM and OKC. However, evaluation of other effective growth factors is also imperative

Keywords: epidermal growth factor receptor (EGFR), Ameloblastoma (AM), Odontogenic Keratocyst (OKC), odontogen

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Evaluation of Frequency of Mortality and Risk Factors in Patients with Acute Myocardial Infarction referring to Peymanieh Hospital, Jahrom, Iran During the Years 2013-2017 (Research Paper)

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Introduction: Coronary artery disease is one of the most common and most dangerous causes of mortality. Given the effect of modifiable risk factors such as diabetes and hypertension in the outbreak of heart diseases, the development of cardiovascular diseases can be prevented by controlling risk factors and improving lifestyle. This study aims to evaluate the frequency of mortality and risk factors in patients with acute myocardial infarction

Methods: This cross-sectional descriptive study was conducted on 500 medical records of patients with myocardial infarction in Jahrom University of Medical Sciences hospitals. The demographic characteristics of the subjects (age, sex, marital status, etc.) and the final status of patients after a heart attack, the presence of various risk factors including hypertension, diabetes, hyperlipidemia, and the symptoms that for their reason the patients referred to the hospital were recorded in the data collection form. The data were analyzed using SPSS software.

Results: At first, a sample of 500 people was considered, and according to exclusion criteria, 476 people were finally analyzed. Out of 476 patients, 66.8% were male and 33.2% were female. The mean age of the patients was 64 years. There was a significant association between sex and the rate of myocardial infarction (P-value <.05). There was no significant correlation between age and rate of myocardial infarction (P-value> .05). In this study, 39% of the patients had diabetes, 33% had hypertension and 12.5% had dyslipidemia. Moreover, 5.04% of males and 9.5% of females died after myocardial infarction. Conclusion: Myocardial infarction rate has dropped in recent years, but the prevalence of this disease is still increasing

Conclusion: Myocardial infarction rate has dropped in recent years, but the prevalence of this disease is still increasing

Keywords: Risk Factors, Myocardial Infarction, Mortality

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Evaluation of genetic variations in ACTRT1 gene in patients with acephalic sperm syndrome compared to control group (Research Paper)

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2. Royan In

Introduction: Male infertility is a complex syndrome encompassing a broad spectrum of disorders. Among the significant factors contributing to male infertility is teratospermia, a disorder characterized by abnormal sperm morphology. One rare yet severe form of teratospermia is Acephalic Sperm Syndrome, which is investigated through endocrine evaluation. Acephalic Sperm Syndrome is defined by the presence of headless sperm during ejaculation. Previous research has identified several genes associated with Acephalic Sperm Syndrome, and this study focuses on investigating genetic changes in the ACTRT1 gene. ACTRT1, also known as T-actin-related protein or ARPT1, is specifically expressed in the testis and encoded by the ACTRT1 gene.

Methods: For this research, samples were collected from 10 infertile men with acephalic sperm and 10 healthy men with normal morphology serving as the control group. DNA extracted from blood samples in both the case and control groups was amplified using specific primers, and the resulting PCR products were sequenced.

Results: No mutations were detected in the ACTRT1 gene in either group.

Conclusion: Although this study did not establish a relationship between genetic changes in the ACTRT1 gene and sperm acephalic syndrome, further investigation of the gene's promoter region is warranted.

Keywords: genetic variation , acephalic sperm syndrome , ACTRT1 gene

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Evaluation of Heavy Metals (Pb & Cd) in natural clay used in grape juice processing (Research Paper)

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Introduction: Natural clay with the scientific name of bentonite is found in mineral areas in volcanic ash of Iran. Bentonite is a special type of granular clay that is a product of volcanic ash, which contains 08% of Montmorillonite 4 Si8 Al4o2 (OH) 4, nH2o mineral clayThis decolorizing soil reduces red color, reduces chlorophyll, breaks down peroxide and reduces oxidation products such as aldehydes, columns, hydrocarbons and increases the oxidative resistance of oil, absorbs soap and phosphatides and also absorbs heavy metals in the oil. Grape juice has been shown to reduce the acidity of grape juice. Studies have shown that the use of natural clay used in the traditional production of grape juice causes significant amounts of salts to enter the final product, which in the long run can be for the consumer.

Methods: Sultani acid method was used to measure the amount of lead and cadmium in the soil. The concentrations of cadmium and lead in the final solution were read using a PG990 atomic absorption spectrometer.

Results: Laboratory results determined the mean lead concentration was 41 ppm and the mean cadmium concentration was 0.1 ppm, which is lower than the EPA standard limit. Comparison of means in different sources did not show a significant difference.

Conclusion: According to the results of laboratory analysis and statistical analysis, the amount of heavy metals in the above soil is in accordance with the standard. Is more.

Keywords: Natural clay, sap, heavy metals, grape juice

Evaluation of high-strength exercise on Alzheimer's disease using microarray and bioinformatics tools (Research Paper)

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Introduction: Alzheimer's disease, which stands as the most commonly observed cause of dementia, manifests itself through anomalous modifications in the brain, eventually culminating in a drastic deterioration of cognitive faculties and alterations in conduct and personality. Individuals suffering from Alzheimer's disease display a plethora of semantic incapacities, alongside functional inadequacies in the respective domains, which impede the normal activation of cognitive processes. The field of cognitive neuroscience, in its quest to augment comprehension of the fundamental biological mechanisms that underlie Alzheimer's disease, endeavors to formulate and implement preventive and therapeutic interventions premised on the latest research findings. Population aging is a global phenomenon, according to statistics, 1.5 billion elderly people are expected in 2050. On the other hand, Alzheimer's disease is known as the most common cause of neuronal degeneration in the elderly. This disease affects many parts of the brain and causes disturbances in the patient's activities, including memory, thinking, learning speech and judgment. Studies show that the life expectancy of Alzheimer's patients after diagnosis is only nine years. While in 2016, around 47 million people around the world were struggling with dementia. As per the findings of the World Alzheimer's Disease Report 2021, it has been observed that an enormous number of human beings, exceeding 55 million in total, are currently grappling with the complex and challenging condition of cognitive impairment on a global scale. Forecasts show that this number will reach 131 million people in 2050. One of the important parts of the brain that is damaged in Alzheimer's disease is the hippocampus. It has been found that the volume of the hippocampus in Alzheimer's patients decreases by about 3 to 5 percent every year. Decreased hippocampal volume leads to memory

impairment and increased risk of dementia. Considerable scientific data has suggested that environmental variables, such as physical activity and diet, can engender improved cognitive performance. Also has been shown that physical activity can be beneficial for cognitive function in people with neurodegenerative disease, regular activity is associated with various structural changes in the nervous system, especially in the hippocampus. Considering the positive effects of exercise on the health of the elderly, the importance of examining the effect of exercise on these patients is essential. In this study, changes in gene expression, protein network and cellular pathways under the influence of high-intensity exercise on the hippocampus were investigated and compared with Alzheimer's disease.

Methods: Hippocampal tissue microarray data (effective high-intensity exercise) in GEO database were analyzed by GEO2R online software. DiseGeNET database employed for the increased genes expressed were examined with Alzheimer's disease-related genes. Also, STRING database was used to examine protein connections, then the resulting network was analyzed with Cytoscape software. The Enrichr database was also used to examine cellular pathways.

Results: The results showed that nearly 20 percent of the increased expression genes in high-strength are associated with Alzheimer's disease. Among them, three genes ARGGAP36, PDYN and HLA-DQA1 had the highest expression and in protein network analysis, SNAP25, SYT1 and GABRG2 proteins had the highest degree. Also, with increasing sports activity, the amount of neuronal growth factors increases. On the other hand, MAPK and cAMP cell pathways are activated.

Conclusion: Increased exercise increases the expression of growth factors and genes related to calcium homeostasis in the hippocampus. But it also activates cellular pathways such as MAPK and cAMP. It seems that managing these cellular pathways can improve the beneficial effect of exercise on Alzheimer's disease.

Keywords: neuro cognitive disease ,Alzheimer's disease, exercise, microarray, hippocampus

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Evaluation of IDH1 and IDH2 gene mutations in Acute Myeloid Leukemia patients (Research Paper)

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Introduction: Acute myeloid leukemia (AML) is characterized by clonal expansion of malignant myeloid blast cells in the bone marrow with impaired normal hematopoiesis. AML is a hematopoietic disorder characterized by multiple cytogenetic and molecular abnormalities and accounts for 25% of childhood leukemia diagnoses. The prognosis of childhood AML remains poor, with a recurrence rate of approximately 30%. Therefore, to increase the efficiency of treatment, new treatment approaches are necessary. A common feature in AML is an altered epigenetic pattern resulting from somatic mutations in epigenetic regulators or specific translocations that interfere with the normal epigenetic program. Several important molecular markers such as IDH1/2, FLT3, NPM1 and CEBPA mutations have been identified in the prognostic classification of AML with normal cytogenetics (CN-AML), Mutations in these genes have been shown to have clinically significant prognostic value. Isocitrate dehydrogenases (IDHs) are a group of enzymes that convert isocitrate to α-ketoglutarate (α-KG) in two steps in the Krebs cycle (TCA). Driving mutations in IDH1 and IDH2 have been observed in several tumors including glioma, AML, myeloproliferative neoplasm, chondrosarcoma, lymphoma, melanoma and thyroid cancer. As a result of these mutations, an oncometabolite called hydroxyglutarate is produced, which plays a role in tumorigenesis. The purpose of this study is to investigate the mutation rate of IDH1/2 genes in AML patients of Shariati Hospital in Tehran and the relationship of these mutations with other genetic mutations of FLT3 and NPM1.

Methods: At first, DNA of AML patients was extracted from peripheral blood (PB) and bone marrow (BM) samples. Then, using the HRM technique, the mutation rate of IDH1/2 genes in these patients was investigated and compared with the DNA sample purified from the blood of a healthy person (Wild Type).

Results: In the conducted study, the presence of IDH1 and IDH2 mutations was investigated by HRM molecular method. Among the 88 sample cases, 15 cases (17%) of mutated IDH1 and 16 cases (18%) of mutated IDH2 were observed. In this study, statistically significant relationship between IDH1/2

mutation and FLT3 mutation and platelet count (Plt) was not observed (P value>0.05). However, a significant relationship between IDH1 mutation and NPM1 mutation, overall survival (OS) and white blood cell (WBC) count was observed (P value<0.05), also in this study, IDH2 mutation did not show a significant relationship with overall survival (OS) and WBC count (P value>0.05).

Conclusion: In general, in this study, only NPM1 mutation, WBC count and overall survival rate (OS) were significantly correlated with IDH1 mutation, but no significant correlation was observed between any of the mentioned variables with IDH2 mutation.

Keywords: AML, IDH, NPM1, FLT3, OS, Plt, WBC.

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Evaluation of protective effect of resveratrol loaded solid lipid nanoparticles on reducing radiation-induced or doxorubicin injection damages on mice spermatogenesis system. (Research Paper)

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Introduction: Resveratrol (RES), a naturally occurring polyphenol known as 3,4',5-trihydroxystilbene. Remarkably, RES has been identified in over 70 plant species. Extensive research has uncovered a multitude of therapeutic benefits associated with RES, encompassing antioxidant, anti-hyperlipidemic, immuno-modulatory, anti-platelet, anti-inflammatory, anti-carcinogenic, neuroprotective, vasorelaxant, and cardioprotective effects.. Radiotherapy and chemotherapy are widely employed therapeutic approaches for cancer management. While these treatments have demonstrated favorable outcomes in cancer control, it is crucial to recognize that they can impart deleterious effects on non-cancerous cells, thereby instigating a cascade of undesired events such as heightened oxidative stress within cellular systems. Undoubtedly, the manifestation of these side effects can considerably impact the quality of life for patients. Consequently, the imperative pursuit of discovering and developing novel, efficacious compounds that can mitigate these adverse effects and protect normal tissues should be given utmost priority. New ways have been opened to increase the efficacy of the therapeutic effects of the molecules by nano drug delivery system, Especially Solid lipid nanoparticles (SLN) have reported to be as promising nanocarriers in cancer therapy SLN have reported to be as promising nanocarriers in cancer therapy. The purpose of this study was to evaluate protective effects of resveratrol as an antioxidant agent loaded by Solid lipid nano particles against toxicity of induced radiation and doxorubicin (as a chemotherapy drug) in

testis tissue. In recent years, novel approaches have emerged to enhance the therapeutic efficacy of molecules through nano drug delivery. Solid lipid nanoparticles (SLN) have gained significant attention as potential nanocarriers for cancer treatment. The objective of this research was to assess the protective properties of resveratrol, an antioxidant agent encapsulated within Solid lipid nanoparticles, against the detrimental effects of radiation-induced toxicity and doxorubicin, a chemotherapy drug, on testicular tissue.

Methods: Solid lipid nanoparticles (SLNs) were generated through the utilization of high shear homogenization. The physicochemical characteristics of the SLNs were assessed employing Dynamic Light Scattering (DLS), which provided measurements for the average particle size and Zeta-potential to gauge the stability of the nanoparticles in suspension. Additionally, scanning electron microscopy (SEM) was utilized to evaluate morphological properties. The release of the drug was investigated by means of a dialysis bag with a molecular weight cutoff of 20 kD. To examine the cytocompatibility of SLN, RES, and RES-SLN, the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay was performed. Furthermore, the chemical interactions among different functional groups were assessed using FT-IR spectroscopy through the employment of the potassium bromide disk method. In this experiment, a total of 60 adult male mice, aged 4-5 weeks and weighing between 25-35g, were utilized. The mice were classified into six different groups, and their oxidative stress parameters were evaluated. The first group, referred to as the control group treated with normal salin 0.9%. The second group was administered a dosage of 3 mg/kg of DOX every other day for a duration of three days. The third group was exposed to a radiation dose of 2 gray (Gy) at a rate of 300 cGy per minute. The fourth group received a daily dosage of 10 mg/kg of SLN-RES for a duration of seven days. The fifth group underwent a combined treatment involving a dosage of 3 mg/kg of DOX every other day for three days then 10 mg/kg of SLN-RES per day for seven days. Lastly, the sixth group was subjected to a daily dosage of 10 mg/kg of SLN-RES for seven days, befor a radiation dose of 2 Gy. Subsequently, the assessment of the induced damage caused by radiation and DOX, as well as the protective effects of RES-SLN, was carried out by evaluating the levels of malondialdehyde (MDA) and the activity of superoxide dismutase (SOD) in the testis tissue.

Results: The findings suggest that RES-SLNs exhibit an average size of 246nm, demonstrating favorable stability characterized by a zetapotential of -15mV. Moreover, SEM imaging confirms the spherical nature of the nanoparticles. Notably, the encapsulation efficiency (EE) and drug loading

(DL) rates were determined to be 72% and 12%, respectively. Furthermore, the cytocompatibility of RES-SLN with fibroblast cells was validated through the MTT assay, affirming its safety for in vivo biomedical applications. The findings of this study highlight that the irradiation and administration of doxorubicin led to a substantial elevation in the level of MDA within the testes of mice. Nevertheless, the injection of RES-SLN displayed a restorative effect, effectively bringing the MDA levels back to baseline. Furthermore, the activity of SOD exhibited a notable decline in the irradiated and doxorubicin-treated group. However, following the injection of RES-SLN, the SOD activity returned to the levels observed in the normal group.

Conclusion: In conclusion, the utilization of RES-SLN demonstrates its capacity to shield the testes of mice from the detrimental consequences of irradiation and doxorubicin while showcasing significant promise within the realm of clinical application.

Keywords: Radiation, Doxorubicin, Resveratrol, Solid lipid nanoparticle, Spermatogenesi, MDA, SOD

Evaluation of the anticancer effect of gel filtration chromatography fractionation from cobra venom on glioblastoma cancer (Research Paper)

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Introduction: cancer is the most common cause of death from the disease in the world (1,2). Metastasis is the leading cause of cancer mortality (3,4). Metastasis occurs in 20% of patients suffering glioblastoma. Cancer cells transfer from the brain to different parts of the body including the lung, chest and colon (5). Glioblastoma is the most deadly from of the tumor (6,7). Although glioblastoma occurs in the brain stem cerebellum and spinal cord (8). there are many therapeutic methods available today but the mortality rate from glioblastoma cancer is very high in both adults and children (9). Therefore the human are looking natural resources such as poisonous animals that have the least side effects to treat cancer (10). Snake venom contains several different proteins, enzymes, peptides and nucleotides (11,12). Each snake venom is different the researchers observed that the venom varied in different species according to the age of the snake and the climate in which they lived (13). Cytotoxicity of various compounds of snake venom causes changes in cellular metabolism which leads to several effects on cancer cells (14). Gue et al. studied the cytotoxins from Chinese cobra venom in rabbits (15). Zhang et al. isolated 98 KD proteins containing two subunits from Agkistrodon acutusl snake venom that proteins could induces apoptosis (16). Gomes et al. isolated cardiotoxic killer protein from cobra venom. They used ion exchange chromatography and Hplc (17). Sumitra et al. observed that phospholipase A2 from Indian cobra venom inhibitis cancer cells (18). Lafnoune et al. studied the effect of cobra venom on Hepatocellular carcinoma (19). Humans, Have been thinking of making medicine from natural sources (20). The purpose of this investigation isolated proteins or peptide from Iranian cobra venom which has a high lethality of glioblastoma cancer cells.

Methods: At the first we lyophilized cobra venom (21). The prepare venom, we mixed 50 mg of venom with 300 µl of water inside a microtube and

determined the concentration by the BCA method (22). Then we did SDS-PAGE an assay to determine the molecular weight of the proteins (23). To separate the venom of the cobra, we did FPLC (24). All fractions were lyophilized and concentration was determined BCA. The molecular weight of the protein determined SDS-PAGE. Then the cell culture of U87MG cell line was done and using the MTT test. The protein with the highest lethality of brain cancer was obtained

Results: Based on the results, it was observed that fraction 2 up to concentration 5 µg/µl had a more lethal effect than other fractions, so it can be concluded that fraction 2 has the ability to kill brain cancer cells by 99%.

Conclusion: Glioblastoma is a lethal and heterogeneous tumor (26). The survival rate of the affected person is only 5% for more than 5 years (27). Today many pharmacists use the venom of poisonous animals to make medicine (28). Snake venom has compounds that cause apoptosis (29,30). The first study was conducted by Bragance and et al on the effect of Naja Naja snake venom on sarcoma cancer cells (31,32). In 1997, Ahn and et al examined cobra venom on stomach cancer cell line and observed that cancer cells were destroyed by 74% (33). But in our research , brain cancer cells were destroyed by 99%. In this research we were able to find a fraction that kills 99% of brain cells. We also hope that using this fraction a drug or a method to deal with glioblastoma cancer.

Keywords: Brain cancer, Cobra venom, Chromatography, MTT assay, Cell culture.

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Evaluation of the compliance of the presented and implemented lesson plans of the basic medical sciences course at Abadan University of Medical Sciences (Research Paper)

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Introduction: The lesson plan is one of the most important factors involved in the process of students' education, which, in addition to improving their views on the quality of education, also makes the activities of students and professors more targeted. The current study was designed and carried out to evaluate the degree of conformity of the lesson plan presented and implemented by the Basic Sciences Department of Medicine.

Methods: In this descriptive-analytical study, which was conducted cross-sectionally in the second semester of 1399-1400, 176 students of general medicine at the basic science level participated. The lesson plans of all basic medical science courses were examined. At the beginning of the semester, all the lesson plans were uploaded to the website of “Tabib” by the lecturers. The degree of conformity of the lesson plan with the teaching style of the lecturers was recorded based on the opinion of the students and using a 20-question questionnaire. In the end, the obtained data were analyzed based on the Chi-square and Fisher test and using STATA version 14 software.

Results: The degree of compliance in all studied areas was 70% or higher, except for “Teaching method and presented lesson plan” and “Education content and presented lesson plan”. The highest level of conformity was observed in “Teaching aid methods and lesson plans provided”, so 77% had acceptable compliance and 50% had good and excellent compliance.

Conclusion: According to the obtained results, it can be concluded that the compliance rates of the presented with implemented lesson plans were optimal. Considering the importance of the subject, it is better to improve the quality of lesson plan presentations by continuous training of lecturers in the form of educational workshops.

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Keywords: Lesson Plan, Lecturers, Compliance

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Evaluation of the dietary zinc association with Gallstone Disease in women: a case-control study (Research Paper)

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Introduction: Gallstone disease (GD) is a common health problem associated with the gastrointestinal tract. Considering that diet has been recognized as an amendable risk factor for GD, this study was performed to define the association between dietary zinc intake with GD risk among Iranian female patients.

Methods: This case-control study was conducted among women including 75 patients with GD and 75 healthy controls in the Gastroenterology and Hepatology clinic of Taleghani Hospital in Tehran, Iran from October 2020 to March 2021. A validated, semi-quantitative food frequency questionnaire was used to evaluate the usual intake of participants. The Nutritionist IV software that was upgraded for Iranian foods was used to assess the registered foods. To find the best predictors of GD, multivariate logistic regression was used. This study was approved by the Ethical Committee of the Faculty of Nutrition and Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran (research ethics number: IR.TBZMED.REC.1398.1202).

Results: The results of the analysis showed an inverse significant association between dietary zinc intake (odds ratio: 0.75; 95% confidence interval: 0.58–0.98; P=0.036) with GD. No significant association was observed between other dietary minerals and GD.

Conclusion: Present results suggested that higher dietary zinc was associated with a lower risk of GD. To support these findings more studies are required.

Keywords: Gallstone disease, Common bile duct stone, Dietary zinc

Evaluation of the Effect of the Cytarabine drug on Expression of HOXA-AS2 in Acute lymphoblastic leukemia (Research Paper)

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Introduction: Children, adolescents, and young adults comprise 70% of ALL cases. The incidence of ALL in United States (US) is 1.8 per 100,000 for all age groups and 5 per 100,000 for ages 0–19. While the incidence in Europe is comparable to the US, data suggest higher incidence in Mexico and other Latin American countries. Survival in ALL is strongly influenced by age with five-year overall survival being 80% in <50 years and <35% in >50 years. T-ALL comprises 15–25% of ALL cases in children and adults. Therefore, T-ALL is primarily a disease of children and young adults and rare in older adults. Sequential accumulation of genomic lesions in the immature T cell progenitors culminates in leukemic transformation and a high proliferative index translates clinically to leukocytosis and extramedullary disease, including large mediastinal/thymic masses and central nervous system (CNS) involvement. The genomic and molecular aberrations seen in T-ALL are distinct from that of B-ALL, yet, up until recently, similar treatment regimens were used for both diseases. The distinction between T-ALL and T-lymphoblastic lymphoma (T-LBL) depends on the degree of bone marrow involvement, with T-ALL cases defined by 20% or more blasts in the bone marrow, whereas T-LBL cases have less than 20% bone marrow blasts with predominance of extramedullary disease. One of the most successful and often used antineoplastic medications is still cytarabine. Arac 's unique metabolism and inactivation by aldehyde dehydrogenase are responsible for its distinct cytotoxic properties. This study aimed to see how cytarabine affected the expression of the HOXA-AS2 gene in acute lymphoblastic leukemia.

Methods: In this research, Two Arac concentrations were created for the current study: 1 and 5 µM at 24 hours. After purchasing the Jurkat E6.1 cell line from the Pasteur Institute, it was given a prepared dose of Arac 24 hours

after cell passage. Following RNA extraction and cDNA synthesis, Real-Time PCR was used to examine the changes in the expression of HOXA-AS2 and GAPDH.

Results: The results of our findings showed that the expression of HOXA-AS2 in comparison with the GAPDH housekeeping gene decreased after 72h of Arac treatment at both of the concentration drugs. According to the findings, changes in HOXA-AS2 gene expression decreased after 24 hours at a concentration of 1µM and 5µM decrease were statistically significant These changes included 1µM (0/903) and 5µM (0/868) at 24 hours, respectively. (P <0.001)

Conclusion: According to the present study results, alternation in HOXA-AS2 expression after treatment with Arac, at two concentration were effective in the decrease of HOXA-AS2 expression. Evidence showed that Arac has positive potential and efficacy because the drug was effective in decreasing gene expression in both concentrations in 24 hours. Therefore, Arac can be a useful drug in controlling the expression of genes involved in leukaemia.

Keywords: Acute lymphoblastic leukaemia, LncRNA, HOXA-AS2, Cytarabine

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Evaluation of the Effect of the Mercaptopurine drug on Expression of HOXA-AS2 in Acute lymphoblastic leukemia (Research Paper)

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Introduction: The most typical kind of teenage cancer is leukaemia. Acute lymphocytic leukemia (ALL), makes up around 78% of all. Mercaptopurine is used alone or with other chemotherapy drugs to treat acute lymphocytic leukaemia (ALL; also called acute lymphoblastic leukaemia and acute lymphatic leukaemia; a type of cancer that begins in the white blood cells). Mercaptopurine is in a class of medications called purine antagonists. It works by stopping the growth of cancer cells. The enzyme thiopurine S-methyltransferase (TPMT) is responsible, in part, for the inactivation of 6-mercaptopurine. TPMT catalyzes the methylation of 6-mercaptopurine into the inactive metabolite 6-methylmercaptopurine this methylation prevents mercaptopurine from further conversion into active, cytotoxic thioguanine nucleotide (TGN) metabolites. Certain genetic variations within the TPMT gene can lead to decreased or absent TPMT enzyme activity, and individuals who are homozygous or heterozygous for these types of genetic variations may have increased levels of TGN metabolites and an increased risk of severe bone marrow suppression (myelosuppression) when receiving mercaptopurine. This study aimed to see how Mercaptopurine affected the expression of the HOXA-AS2 gene in acute lymphoblastic leukaemia.

Methods: In this research Two 6mp concentrations were created for the current study: 5 and 10 µM at 24 hours. After purchasing the Jurkat E6.1 cell line from the Pasteur Institute, it was given a prepared dose of 6mp 24h after cell passage. Following RNA extraction and cDNA synthesis, Real-Time PCR was used to examine the changes in the expression of HOXA-AS2 and GAPDH.

Results: The results of our findings showed that the expression of HOXA-AS2 in comparison with the GAPDH housekeeping gene decreased after 24h of 6mp treatment at both of the concentration drugs. According to the findings, changes in HOXA-AS2 gene expression decreased after 24 hours at a concentration of 1µM and 10µM decrease were statistically significant These changes included 5µM (0/915) and 10µM (0/766) at 24 hours, respectively. (P <0.001)

Conclusion: According to the present study results, alternation in HOXA-AS2 expression after treatment with 6mp, at two concentration were effective in the decrease of HOXA-AS2 expression. Evidence showed that 6mp has positive potential and efficacy because the drug was effective in decreasing gene expression in both concentrations in 24 hours. Therefore, 6mp can be a useful drug in controlling the expression of genes involved in leukaemia.

Keywords: Mercaptopurine, Acute lymphoblastic leukaemia, LncRNA, HOXA-AS2

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Evaluation of the Effect of the Ni-Thiosemicarbazones complex on Expression Changes of CPEB2 gene in Acute lymphoblastic leukemia (Research Paper)

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Introduction: The aberrant proliferation and differentiation of a clonal population of lymphoid cells are involved in the pathogenesis of ALL. ALL has a poor prognosis, with only 10% of adult ALL patients surviving and 30% of pediatric ALL patients surviving. The complete remission rate in adult ALL is 30 percent to 40 percent in the first relapse and 20 to 25 percent in the second relapse with conventional chemotherapy. CPEB2 is increased in cancer tissues and increases the proliferation and migration of cancer cells of this kind. Thiosemicarbazones (TSCs) are a type of Schiff base made by combining thiosemicarbazone with an appropriate aldehyde or ketone. Chemists and biologists have been studying TSCs because of their diverse pharmacological properties. The application of these outstanding metal chelators against cancer is one of the promising areas in which they are being developed. The goal of this study was to see how Ni-thiosemicarbazone complexes affected the expression of the CPEB2 gene in a cell line that had been diagnosed with acute lymphoblastic leukemia.

Methods: In the current research, two concentrations of Ni-Thiosemicarbazone complexes were prepared: 51µM and 61µM at 48h. The Jurkat E6.1 cell line was purchased from Pasteur Institute and treated with prepared doses of the Thiosemicarbazones complexes Ni at 24 and 48 hours after cell passage. The expression changes of CPEB2 and GAPDH were studied using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to draw the diagrams.

Results: The results of our findings showed that the expression of CPEB2 in comparison with the GAPDH housekeeping gene increase after 48 hours of Ni-Thiosemicarbazone complexes. According to the findings, changes in CPEB2 gene expression increased after 48 hours at a concentration of 51µM and 61µM were changes expression included 51µM (1.243) and 61µM (1.502) at 48 hours, respectively. (P <0.001)

Conclusion: According to the present study results, alternation in CPEB2 expression after treatment with Ni-Thiosemicarbazone complexes, at tow concentration were ineffective in decrease of CPEB2 expression. Evidence showed that the Ni-Thiosemicarbazone complexes does not have positive potential and efficacy because the drug was ineffective in decreasing gene expression in tow concentrations in 48 hours (p-value 0.001). And it is suggested to study the mentioned gene in order to further investigate the therapeutic potential of Ni-Thiosemicarbazone complexes in other concentrations and times.

Keywords: Ni-Thiosemicarbazones complexes, CPEB2, GAPDH, Acute lymphoblastic leukemia

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Evaluation of the Effectiveness of Chemotherapy on Metastatic Breast Cancer and HRD Biomarkers and Pathogenicity of BRCA1/2 in this Disease with Focusing on the Usefulness of Exome Sequencing (Review)

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Introduction: Breast cancer (BC) is the most common cancer diagnosed in women worldwide. In 2023, there were about 43,700 deaths (43,170 women and 530 men) due to breast cancer in the United States. Worldwide breast cancer is the fifth leading cause of death. Women with BRCA1 or BRCA2 gene mutations are at risk for breast and ovarian cancer and often undergo surgery to remove both of their ovaries. Mutations in the BRCA1 and BRCA2 genes account for 50% of inherited BC and up to 10% of BC. Triple negative BC (TNBC) accounts for 15% of BC in the early stages and is associated with poor long-term results compared to other BC subtypes. TNBC is enriched for BRCA germline mutations and is the basis for the use of molecular testing as a biomarker to identify patients. Identification of unclassified BRCA variants of unknown importance (VUSs) Clinical usefulness of molecular testing limits the risk issues associated with computation VUS are mainly undesirable types that lack of experimental and clinical data cannot be categorically classified as pathogenic. The American College of Genetics and Medical Genomics (ACMG) says that efforts should be made to resolve the classification of this variant as pathogenic or benign. While the role of BRCA1/2 genes in familial breast and ovarian cancer is well established. With the development of poly (ADP-ribose) polymerase (PARP) inhibitors, the exact relationship between BRCA1/2 genes and triple-negative sporadic breast cancer/high-grade serous carcinoma (TNBC/HGSC) needs further investigation. The aim of this study was to determine a specific clinical pathway for VUS carriers and to investigate the biomarkers of genomic instability and their relationship with the prevalence of BRCA1/2 and CNA somatic spot mutations.

Methods: This interventional study with narrative review approach was conducted in 2023 by searching keywords such as Chemotherapy, Metastatic Breast Cancer, HRD Biomarkers, Exosome and BRCA1/2 in valid databases such as: Scopus, Science Direct, Web of Science, and PubMed.

Results: Metastatic breast cancer (MBC) is often managed with platinum-based chemotherapy during the course of the disease. The benefits of these treatments in the advanced stages of the disease and in non-triadic negative subtypes are not known. Because homologous recombinant deficiency (HRD) can provide information about tumor susceptibility ‹BRCA tumor suppressor genes maintain DNA integrity and allow double-stranded DNA breaks to be repaired by the homologous recombinant (HR) system. Disruption of BRCA protein activity due to pathogenic types of loss of function (LoF) can compromise the effectiveness of the repair system and lead to an increased risk of cancer. Harmful BRCA changes have been associated with an increased risk of various types of cancer, including ovaries, pancreas, prostate, and melanoma. Genetic testing for BRCA genes represents a targeted strategy with clinical management of BC and pathways to prevent relatives of patients. The findings of VUS should be interpreted as non-informational and should not directly affect cancer management. Individual screening and prevention strategies are useful in such cases, overall response rate, disease control rate, PFS and PFS2/PFS1 ratios were evaluated to assess the effectiveness of platinum-based chemotherapy. BRCA1 c.5057A>C (p.His1686Pro) was also detected during oncological evaluations in this study. This mistaken change is located in exon 16 of the BRCA1 gene and has resulted in the replacement of histidine to proline at the amino acid position p.1686 with a 46% allele frequency. The BRCA1 variant c.5057A>C (p.His1686Pro) is annotated in the original public database as a rare VUS (rs730882166). In a single-center study, BRCA1/2 mutation status, HRD score and signature level 3 were reported by multivariate analysis, only the absence of liver metastases independently was associated with better PFS in platinum-based chemotherapy. The exome tumor sequencing method to quantify HRD should be systematically investigated and more valid and standardized before its clinical use. Further studies are needed to confirm these results to guide the use of platinum in MBC.

Conclusion: With multivariate analysis, only the absence of liver metastases independently was associated with better PFS in platinum-based chemotherapy. However, the exome tumor sequencing method to quantify HRD must be systematically investigated and validated and standardized before its clinical use. Further studies are needed to confirm these results to guide the use of platinum in MBC.

Keywords: Chemotherapy, Metastatic Breast Cancer, HRD Biomarkers, Exosome and BRCA1/2

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Evaluation of the role of diffusion-weighted MRI in differentiating benign and malignant ovarian lesions (Research Paper)

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Introduction: Ovarian malignancies are one of the most common cancers of the female reproductive system and account for approximately 5% of women's deaths due to cancer, which requires early diagnosis. Therefore, the purpose of this study is the role of MRA emission weight imaging in differentiating malignant from benign ovarian lesions.

Methods: This study was conducted on 58 patients, of these 31 (53.4%) had benign and 27 (46.6%) had malignant masses. Imaging findings were reviewed in patients. Then the data was analyzed based on the findings of diagnostic accuracy.

Results: The findings of our study showed that the average T2 in patients with malignant tumors were significantly lower than the patients with benign mass (432.87 vs. 687.56) and also the average ADC in patients with malignant tumors were significantly lower. It was less than the patients with benign mass (115.69 vs. 995.39), on the other hand, the mean DWI in patients with malignant tumors was significantly higher than the patients with benign mass (548.03 vs. 184.71) and the average T1+ GAD in patients with malignant tumor was significantly more than patients with benign mass (154/16 vs. 24/44) and finally it was found that DWI and T1+GAD had the highest diagnostic accuracy in diagnosing ovarian malignant masses.

Conclusion: Considering the very high diagnostic accuracy of DWI and T1+GAD factors, malignant tumors can be distinguished from benign tumors with almost 100% accuracy from these two factors and the treatment process can be based on it.

Keywords: MRA Diffusion Weight Imaging, Ovarian masses, Diagnostic accuracy

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Evaluation of trend drugs loaded in lipid nanoparticles in Alzheimer's disease: benefits, challenges and administration route (Review)

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Introduction: Alzheimer's disease (AD) is the most common form of dementia, affecting about 50 million people worldwide prevalence. Accumulation of amyloid-beta plaques and neurofibrillary tangles containing tau protein in the brain is the hallmark pathologies of this progressive neurodegenerative disease that leads to neuronal dysfunction and loss. No current treatments can halt or reverse the progression of AD because the blood-brain barrier (BBB) is an obstacle to the transport of therapeutic agents to the brain. Lipid nanoparticles such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs) have shown promise as drug delivery systems to improve transport across the BBB. Encapsulation of drugs in lipid nanoparticles protects cargo, increases solubility, controls release rate, and may facilitate uptake into the brain through receptor-mediated transcytosis. Many small molecule drugs, peptides, proteins, siRNA, and metal-based agents with therapeutic potential for AD are being incorporated into lipid nanoparticles to test their efficacy after targeted delivery to the brain. This review evaluates and introduces a comprehensive list for trend drugs loaded on lipid nanoparticle technology to deliver for AD candidates. The benefits and challenges of this nanomedicine approach to AD will be discussed, along with the administration routes to determine the impact of in vivo efficacy of nanoparticle drug delivery for AD treatment.

Methods: A complete search strategy was assigned to identify relevant articles based on keywords including drugs, lipid nanoparticles, and Alzheimer's disease and related keywords. PubMed, Web of Science, Scopus, and Google Scholar as popular databases were searched for articles published from 2018 to 2023. The articles were skimmed by two reviewers separately, based on title/ abstract. All relevant studies were included. Unrelated and non-English articles were excluded and listed.

Results: Based on recent investigations, a wide variety of small molecule drugs, biologics, and genetic materials are being actively explored using lipid nanoparticle delivery systems for potential Alzheimer's therapy. These drugs include curcumin, resveratrol, selenium, coenzyme-Q10 (with anti-inflammatory and antioxidant properties), exendin-4 (A glucagon-like peptide-1 agonist for AD diabetic patients), and some anti-amyloid drugs like statins, simvastatin, doxorubicin, cilostazol, anti-amyloid antibodies, and siRNA. Investigations indicate some inhibitor drugs for acetylcholinesterase, phosphodiesterase, histone deacetylase and angiotensin receptor including tacrine, rivastigmine, cilostazol, phenylbutyrate and telmisartan are useful in AD patients respectively. Researchers confirm some naturally secreted hormones (e.g., estrogen, melatonin, and pregnenolone) can positively impact your overall memory and cognitive function. On the other side of the review, common administration routes for drug delivery include oral, ocular, and intranasal (IN) administration, intravenous and intraventricular/intrathecal injection, and transdermal patches are listed. The non-invasive oral and nasal routes and intravenous administration seem to be among the most promising approaches for using lipid nanoparticles to deliver drugs for AD treatment. Overall, IN administration seems to offer direct brain targeting, a non-invasive and suitable route for a vast range of drugs loaded on lipid nanoparticles.

Conclusion: As the results indicated, the most of the drugs are bioavailable to load on lipid nanoparticles which are listed in this review. It should be noted that according to the AD pathogenesis, the drugs chosen. In this way, the most challenge is to administrate and optimize the drug delivery route. When comparing administration routes for drug delivery in AD treatment, there is no definitive "best" option. Each route has different pros and cons in terms of invasiveness, ability to cross the blood-brain barrier, targeted delivery, patient compliance, and suitability for certain drug formulations. Investigations indicate that IN administration is better than others. It appears a promising route as provides direct access to the brain. Besides challenges such as low bioavailability, toxic contaminants, high variability, etc. which require careful formulation strategies using absorption enhancers, optimized delivery devices, enzyme inhibitors, and nanoparticles like liposomes that can protect drugs and modulate transport.

Keywords: Lipid Nanoparticles, Alzheimer disease, Drug Delivery Systems, Intranasal Administration

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Evaluation the Effect of Methotrexate on Expression Changes of TUG1 in Acute Lymphoblastic Leukemia (Research Paper)

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Introduction: In acute lymphoblastic leukemia (ALL), early lymphoid pioneer cells multiply and take the place of healthy hematopoietic cells in the bone marrow. Acute lymphoblastic leukemia (ALL) is mainly a disease of childhood that arises from recurrent genetic insults that block precursor B and T cell differentiation and drive aberrant cell proliferation and survival. Recurrent defects including chromosomal translocations, aneuploidies, and gene-specific alterations generate molecular subgroups of B- and T-ALL with differing clinical courses and distinct responses to therapy. Recent discoveries arising from genome-wide surveys and adoptive transfer of leukemia-initiating cells have uncovered multiple gene copy number aberrations and have yielded new insight into at least one type of ALL-originating cell. Methotrexate, formerly known as amethopterin, is a chemotherapy agent and immune-system suppressant. It is used to treat cancer, autoimmune diseases, and ectopic pregnancies. Types of cancers it is used for include breast cancer, leukemia, lung cancer, lymphoma, gestational trophoblastic disease, and osteosarcoma A purine analog called methotrexate is used to treat autoimmune disorders and leukemia. It has both immunosuppressive and anticancer properties. in leukemia, methotrexate suppresses the activation of nuclear factor. This study set out to investigate the effects of methotrexate on the expression of the LncRNA TUG1 in acute lymphoblastic leukemia.

Methods: In this study, methotrexate was prepared at 1 and 10µM doses. After cell passage, the Jurkat E6.1 was prepared from Pasteur Institute of Iran at the passage I was then treated with methotrexate at 48 h with indicated concentrations. Then RNA extraction and cDNA synthesis were done and the expression changes of TUG1 and the Housekeeping GAPDH were evaluated

by Real-Time PCR. Finally, the results of Real-Time PCR were analyzed by Rest 2002 Software.

Results: our findings discovered that after 48h of treatment with methotrexate at 1µM, the expression of LncRNA TUG1 was considerably lower than in non-methotrexate samples and compared with the reference gene. Conforming to the results, it has been shown of TUG1 at the concentration of 1 and 10µM at 48h were 0.523and 0.712 respectively (P <0.001).

Conclusion: as a conclusion investigation into how the expression of TUG1 changed while it was being treated with methotrexate the doses of 1 and 10µM were unsuccessful in suppressing TUG1 expression. The related results of methotrexate, at in 1 and 10µM, on TUG1 expression for 48h, showed down the expression of the TUG1 tumor suppressor. The result suggests that methotrexate doesn't have enough potential for controlling and treating cancers.

Keywords: Acute Lymphoblastic Leukemia, LncRNA, TUG , Methotrexate

Examining factors predicting the quality of married life of couples: a scope review study (Review)

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1.
2.

Introduction: The quality of married life is a dynamic and important concept that means the mutual relations of couples with each other. This affects all aspects of people's lives. By knowing the factors predicting the quality of married life, we can help to strengthen and strengthen these relationships. The purpose of this study is to determine the factors predicting the quality of married life of couples in a scope-based review study.

Methods: This study in 2022 with steps, study question design, search, which is in the databases of SID, PubMed, Magiran, Iran doc, Science Direct, Scopus and Google Scholar search engine with keywords such as "predictive factors", "marital relations", "Quality of life", "Couples" and their Persian equivalents were carried out and after that, related studies were identified from the period of 2012 to 2022 (the last ten years), the selection of studies, which after screening the title, abstract and full text of 281 studies, finally 18 studies remained to report the results. The studies that had unknown sample size and procedures and their complete content were not available were initially excluded from the study process. The quality screening of the studies was done using the AXIS checklist. Then the results were classified.

Results: The results of the present study are derived from 18 articles that were placed in six categories. The first class is the individual factors that were collected by carefully studying 8 articles and refers to age, education, number of children, length of time since marriage, parenting style, sexual relations pattern of couples. The second class is related to socio-economic factors, where 3 articles mentioned the relationship between financial status, place of residence and job. Psychological factors are also the next category, in 4 articles, the meaning and concept of couples, the individual personality of couples and records of psychiatric disorders such as anxiety disorders were mentioned.Physical - medical factors that include the physical health status of men and women were mentioned in 6 studies. The last class, which represents the cultural factors, includes the view of the woman and her husband on the relationship in the current life, the cultural and religious beliefs of the couple, information sources. An important point in the classification of articles is the overlapping of some articles in several categories.

Conclusion: The quality of married life is related to various factors, and by knowing these factors, it is possible to understand the predictive factors in the quality of married life, and by removing the negative factors and strengthening the positive factors, it helps to strengthen the quality of life in marital relationships.

Keywords: Marital life quality, predictive factors, couples

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Examining LCK and BDNF as Potential Prognostic Biomarkers in Glioblastoma multiforme: Insights from The Cancer Genome Atlas (TCGA)Transcriptomic Analysis (Research Paper)

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Introduction: Introduction: Glioblastoma multiforme (GBM) is a rare but highly malignant brain tumor with a global incidence of fewer than 10 cases per 100,000 people [1]. Despite treatment advances, it remains largely incurable, with a prognosis of only 14-15 months survival post-diagnosis [2]. In this study, we sought to identify genes that impact GBM survival rates in order to uncover new prognostic biomarkers for improved prognosis prediction.

Methods: Methods: In this study, we utilized 'TCGAbiolinks' to access raw RNA-seq data (STAR-Count) and clinical information for Glioblastoma Multiforme (GBM) from TCGA. We identified differentially expressed genes (DEGs) using 'TCGAanalyze_DEA' in combination with edgeR functions, applying stringent criteria (|LogFC| ≥ 2 and FDR = 0.01) for DEG selection. DEGs were organized in a structured table using 'TCGAanalyze_LevelTab,' displaying expression levels in tumor (Cond1type) and normal (Cond2type) samples, along with the 'Delta' value. We enhanced interpretability by replacing gene Ensemble IDs with protein-coding gene names via the 'biomaRt' package and ensured data integrity by eliminating duplicate gene names. Enrichment analysis with 'TCGAanalyze_EAcomplete' revealed associations between DEGs and Gene Ontology (GO) functions and KEGG pathways, identifying over-represented genes or proteins among up-regulated genes. We constructed a protein-protein interaction (PPI) network with the STRING database, analyzing it with Cytoscape, focusing on degree centrality for node evaluation. Finally, we employed the UALCAN database to generate Kaplan-Meier survival curves for hub genes. This streamlined approach

allowed us to comprehensively analyze GBM data, identifying significant genes and pathways.

Results: Results: In an analysis of 175 patients and 60,660 genes, 6,905 Differentially Expressed Genes (DEGs) were identified, with 4,386 up-regulated and 2,519 down-regulated in tumor samples compared to normal. These DEGs were categorized by GO functions into Molecular Functions (MF), Biological Processes (BP), and Cellular Components (CC). In MF, DEGs were significantly associated with channel activity (GO:0015267) with a false discovery rate (FDR) of 1.49e-31. In CC, a notable enrichment of DEGs was found in the plasma membrane part (GO:0044459, FDR 5.67e-62). In BP, cell-cell signaling (GO:0007267) was significantly enriched with an FDR of 6.32e-23. Additionally, KEGG analysis highlighted DEGs' enrichment in the cAMP-mediated signaling pathway (FDR 1.04e-11). Using cytoHubba, the top 10 degree nodes were identified, with only two showing a significant association with poor prognosis based on Kaplan-Meier and log-rank test analysis ($P<0.05$): LCK proto-oncogene (LCK) and brain-derived neurotrophic factor (BDNF).

Conclusion: Conclusions: This study has revealed driver genes and pathways in Glioblastoma multiforme, which may serve as biomarkers and therapeutic targets.

Keywords: Keywords: Glioblastoma multiforme, Biomarkers, Bioinformatics, Gene expression analysis, TCGA

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Examining the challenges caused by the corona pandemic in medical universities (Review)

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Introduction: The 2019 coronavirus pandemic (COVID-19) has brought about many changes in all walks of life and affected the world's medical education system, leading to changes in the conventional teaching methods in most universities. This has especially affected all aspects of education at different levels of education. In line with the management and control of these challenges, solutions have been proposed, many of which can be used in the post-pandemic era. This review examines the challenges, solutions, and achievements caused by the COVID-19 pandemic in the field of medical education.

Methods: This study was conducted using the narrative review method. After studying and evaluating 55 original articles and systematic reviews in international databases and websites: PubMed, Sid, Scopus, Google Scholar, and ISI, and through an advanced and extensive search using the keywords "medical education" and "COVID-19" "students" "Pandemic" during the years 2019 to August 2023 among these retrieved articles in the stages of title, abstract, and full text, finally 20 selected articles were determined and examined.

Results: The findings show that during the pandemic, there were several factors as educational obstacles to educational goals. These factors are classified into four different areas: environment (institution), faculty members, students, and patients. Among these factors, educational barriers related to academic staff constitute the biggest barrier. Acute care programmes with a lack of teaching time have been identified as the most common and relevant barrier to medical education. Subsequently, inappropriate educational environments and insufficient monitoring models have also been identified as educational obstacles. Other challenges include a lack of technology skills, poor time management, and inadequate infrastructure. Due to the rapid development of technology, healthcare education systems must also evolve along with it.

Conclusion: Regardless of the critical conditions of COVID-19, it is critical to identify the challenges and provide crisis management solutions to get out of the crisis, and to pay attention to the opportunities and capacities behind the crisis. Each of the four groups plays an important role in the education process, and efforts should be made to establish proper coordination and cooperation between them.

Keywords: medical education, COVID 19, pandemic, students

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Exosomes and it's role in the prognosis and therapy for prostate cancer (Review)

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Introduction: Prostate cancer is a common cancer in men and primarily affects men over 50 years of age. Prostate cancer is the third most prevalent cancer in men worldwide and the sixth most prevalent in Iran. Since the survival rate for people whose prostate cancer has spread to other parts of their body is low, By using new methods, they can survive longer or even be completely healed.Exosomes, which are extracellular vesicles, have received a lot of attention from oncologists recently.

Methods: Literature Review

Results: The regulation of immune response, cell stability, tissue repair, and cancer progression are just a few of the vital biological functions that exosomes are involved in. Exosomes affect cancerous cells through their communication between cells and the transfer of molecules. Two issues arise when trying to use exosomes to manage cancer treatment: cancer diagnosis and drug delivery system. With respect to the first issue, invasive methods often endanger the life of the patient. By replacing the exosome detection method with an invasive method as a biomarker, these risks can be greatly reduced. On the other hand, exosomes can be a suitable option for drug delivery due to their stability, biocompatibility, permeability, and low toxicity.

Conclusion: Exosomes can be used through drug administration as well as biomarkers for prostate cancer treatment, but further studies are needed for clinical efficacy.

Keywords: Prostate Cancer, Exosome, Diagnostic, Drug Delivery

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Exosomes' concentration and dimensions are altered by the sudden FBS starvation as environmental stress (Research Paper)

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Introduction: The physiological condition, chemical properties, and serum used as a source of growth factors, hormones, and attachment factors can impact the quality, size, and quantity of exosomes derived from cell culture. Exosomes as important components of the intercellular microenvironment have been found to play a role in regulating cell-to-cell communication. Removing fetal bovine serum (FBS) from the culture medium may induce cellular stress and potentially affect exosome biogenesis. To examine how the secretion of exosomes and their properties in stem cells from human-exfoliated deciduous teeth (SHED) are influenced by sudden and gradual serum-free media (SFM).

Methods: The exosomes will be isolated from the culture medium of SHED-MSCs after removing FBS using an Exocib exosome isolation kit (Cibbiotech, Tehran, Iran) following the manufacturer's protocol. We analyzed exosomes from two groups of SHED-MSC with NanoDrop, Bradford, DLS, and AFM.

Results: Both groups exhibited differences in terms of average yield, nanoparticle sizes as determined by DLS, and SHED-MSC-Exos dimensions as observed through AFM analysis.

Conclusion: When cells are deprived of serum, which is known as serum starvation, it acts as a form of environmental stress that decreases their overall cellular activity. The sudden removal of FBS creates tension within the cells and impacts the production and release of exosomes within the cells.

Keywords: Serum-free media (SFM), Exosome, SHED-MSC, sudden SFM, gradient SFM

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Exploration of Key Genes and Molecular Pathways in Cervical Cancer: Insights from Bioinformatics Analysis (Research Paper)

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Introduction: Cervical cancer (CC) ranks as the fourth most prevalent cancer among women worldwide. The urgent need to identify novel biomarkers and unravel underlying molecular mechanisms has prompted this study. Our objectives were to identify key genes and pathways influencing the diagnosis of CC patients, and to shed light on new molecular mechanisms associated with cervical cancer through bioinformatics analysis.

Methods: Proteomics data from published sources were utilized to gather CC-related information. We constructed a protein-protein interaction (PPI) network involving differentially expressed proteins (DEPs) using STRING and Cytoscape technology. The Cytoscape plug-in CytoHubba was employed to identify hub genes.

Results: Network analysis revealed the top seven hub genes: FGA, ITIH2, APO B, A2M, KNG1, VTN, and FN1, which exhibited overexpression in cervical carcinoma cells compared to normal cervical cells. These identified genes may serve as crucial diagnostic biomarkers and potential targets for CC prevention.

Conclusion: Through bioinformatics analysis, this study successfully screened key genes and pathways closely linked to cervical cancer, thereby deepening our understanding of its molecular mechanisms underlying initiation and progression. These findings hold promise in identifying potential therapeutic targets for cervical cancer.

Keywords: Cervical cancer, differential expression proteins (DEPs), biomarker, bioinformatics

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Exploring the Interplay of Hematological Parameters in Breast Cancer: An In-Depth Review of Emerging Research (Review)

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Introduction: Breast cancer is a malignant neoplasm characterized by uncontrolled growth and proliferation of abnormal cells within the breast tissue, most commonly occurring in the mammary ducts or lobules. As a public health concern, it manifests in various histological subtypes, requiring multimodal diagnostic and therapeutic methods. Multifactorial factors influence the etiology of breast cancer, including genetic mutations (like BRCA1 and BRCA2), environment, hormones, and lifestyle. Genetic mutations, such as oncogene or tumor suppressor gene variants, exposure to carcinogens, hormonal imbalances, and inherited genetic predispositions, initiate and promote abnormal cell growth within breast tissue. Metastasizing, or spreading, to other parts of the body, is a devastating aspect of breast cancer physiology. During metastasis, cancer cells invade nearby tissues, enter the bloodstream, and establish secondary tumors in distant organs. There is no doubt that breast cancer is the number one cancer among women worldwide, and early detection is key. Early detection tools like mammography are widely used. There are several types of treatment available, such as lumpectomy, mastectomy, radiotherapy, chemotherapy, hormonal therapy, and immunotherapy. Using hematological factors for diagnosis is a reliable paraclinical method. A patient's hematopathology and follow-up treatment can predict their severity, mortality, and survival.

Methods: Pubmed, Google Scholar and Scopus databases were searched for related studies in the literature.

Results: Several hematological parameters can reflect breast cancer's aggressiveness. Neutrophophil-to-lymphocyte ratios (NLR) and platelet-to-lymphocyte ratios (PLR) have been linked with aggressive tumors. A higher level of these ratios indicates a heightened inflammatory response, which may correlate with advanced disease stages and a less favorable prognosis. During recent studies, platelets, lymphocytes, monocytes, and basophil counts did not differ significantly between breast cancer patients and non-patients. Patients with higher breast cancer stages had higher PLT counts.

Patients also had higher mean WBC, RDW, and MPV. A breast cancer patient's mean RBC, Hb, HCT, MCV, and MCH values were lower than those of a non-patient. Hematological parameters can distinguish breast cancer patients from healthy individuals. Several hematological parameters, including elevated levels of markers like C-reactive protein (CRP), particularly in cases of advanced or metastatic disease, or elevated levels of erythrocyte sedimentation rate (ESR), may indicate inflammation or an underlying malignancy, which should be investigated further. Breast cancer patients may be susceptible to infection or immunosuppression during treatment, which may indicate elevated or decreased WBC counts. It is possible that elevated Erythrocyte Sedimentation Rate (ESR) levels can be a non-specific sign of inflammation, which may be linked to cancer or other health issues. Cancer progression and a poorer prognosis are often linked to chronic inflammation. Certain hematological parameters can be used to predict cancer recurrence. Indicators of recurrence, such as lactate dehydrogenase (LDH) or CA 15-3, are associated with breast cancer. The presence of high LDH levels can indicate tumor growth, metastasis, or tissue damage. In these patients, anemia is a common hematological finding. Cancer-related anemia can be the result of the tumor's adverse effect on the bone marrow as well as chronic inflammation caused by the disease. The inflammatory response of tumors can be a target for treatment. By analyzing peripheral blood, leukocytes, neutrophils, lymphocytes, monocytes, platelets, and derived NLRs (dNLRs), PLRs, and LMRs, many malignant cells show an inflammatory state. Breast cancer can cause paraneoplastic syndromes by secreting substances that affect blood cell production. Hematological abnormalities can be associated with paraneoplastic syndromes, including thrombocytosis (high platelet counts) and leukemia (excessive WBC production). Hematological parameters may be affected by breast cancer treatments, such as chemotherapy. Chemotherapy may result in myelosuppression (suppression of bone marrow) as well as anemia and neutropenia.

Conclusion: As a result, hematological parameters are not only useful in diagnosing breast cancer but can also be used to monitor treatment responses, assess disease progression, and predict prognosis in addition to the initial diagnosis. Comprehensive diagnostics and monitoring can improve the quality of life and outcomes for patients with breast cancer by including these parameters. As an example, a decrease in hemoglobin levels or an increase in platelet counts may indicate metastasis or tumor growth, which indicates a poor prognosis for the patient. To ensure the best possible outcome for breast cancer patients, regular monitoring of these parameters allows healthcare providers to make informed decisions regarding treatment adjustments and supportive care.

Keywords: breast cancer, hematological parameters, breast cancer diagnosis

Exploring the intricacies between drivers of ferroptosis and hematological neoplasms (Review)

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Introduction: Hematologic malignancies comprise a variety of heterogeneous myeloid and lymphoid malignant cells derived from the differentiation block of immortal hematopoietic cells. The majority of patients display avoidance to apoptosis and, ultimately, will face the outcome of chemotherapeutic resistance and recurrence. Ferroptosis induction has been identified as a promising way to cause tumor cell death and overcome treatment failure. The term “ferroptosis” refers to an iron-dependent oxidative form of programmed cell death with the accumulation of lipid hydroperoxides on cellular membranes. It is characterized by unique morphological features and is tightly correlated with various molecular and biological processes, such as iron, amino acid, and lipid metabolism. Cellular pathways can be impacted by ferroptosis either intrinsically or extrinsically. The depletion of glutathione peroxidase 4 triggers the endogenous pathway, while the exogenous pathway can be initiated through the inhibition of cystine uptake or the induction of iron transporters. Excess cytoplasmic Fe2+ promotes ROS and lipid peroxide formation. Various studies have demonstrated that ferroptosis inducers (FINs) are imposed to eradicate malignant cells. The aim of this literature was to summarize the core concept of ferroptosis and to investigate FINs, circular RNAs (circRNAs), long non-coding RNAs (lncRNAs), and their mechanisms of action.

Methods: Multiple searches were conducted on different databases, including PubMed, Scopus, and Google Scholar. Our literature searches focused on studies with terms of “Ferroptosis”, “Xc- cystine transporter”, “LncRNAs”, “CircRNAs”, and “Hematological malignancies”. The search was limited to the years between 2001 and 2023.

Results: Numerous natural compounds, small molecules, and nanoparticles inducing ferroptosis have been able to affect cellular pathways either intrinsically or extrinsically. Likewise, dysregulation of circRNAs and lncRNAs,

the two types of noncoding RNAs, has been related to ferroptosis and lipid peroxidation. The downregulation of circZBTB46 and circ-0000745 genes is related to ferroptosis in AML, while the upregulation of circKDM4C and LINC00618 genes is associated with ferroptosis in ALL and AML, respectively. Ultimately, the overformation of ROS through relevant metabolic processes, which are highly reactive with cellular components, specifically membrane phospholipids, leads to the accumulation of lipid hydroperoxides and cell membrane disorganization.

Conclusion: Findings suggest that induction of ferroptosis is beneficial, but more studies are required to properly comprehend the underlying mechanisms and clinical utility. A deep recognition of the interactions between ferroptosis and hematological malignancies would contribute to the development of effective therapeutic strategies and combination therapies to overcome resistance.

Keywords: Ferroptosis - Xc cystine transporter - LncRNAs - CircRNAs - Hematological malignancies

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Exploring the Therapeutic Effects of Curcumin for Ovariectomy-induced Osteoporosis in Adult Wistar Rats (Research Paper)

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Introduction: Osteoporosis (OP) is a chronic metabolic disease. The present study was conducted to investigate the effect of nanocurcumin on ovariectomy-induced osteoporosis in adult Wistar rats.

Methods: 40 female rats were randomly divided into 5 groups including the control group (rats without ovariectomy and gavage with PBS for two months), SHAM group (rats with ovariectomy and gavage with PBS for two months) and Intervention groups (rats with ovariectomy and gavage with nanocurcumin 50, 100 or 150 mg/kg for two months). Two months after surgery, western blot analyses were performed to evaluate OPG, OCN, and Runx2 proteins in tibia bone.

Results: Regeneration did not occur in the control and SHAM groups, but 50, 100, and 150 mg/kg nanocurcumin groups showed +1, +2, and +3 regeneration, respectively. The expression of osteocalcin in the 100 and 150 mg/kg nanocurcumin groups was significantly higher than the control and sham groups ($p<0.001$) and it was also significantly higher than the 50 mg/kg nanocurcumin group ($p<0.05$ and $p<0.001$, respectively). In the 100 and 150 mg/kg nanocurcumin groups, the expression level of RUNX2 was significantly higher than the control and sham groups ($p<0.05$ and $p<0.001$, respectively) and also significantly higher than the 50 mg/kg nanocurcumin group $p<0.05$ and $p<0.001$, respectively). In the 100 and 150 mg/kg nanocurcumin groups, the expression of osteoprotegerin was significantly higher than the control and sham groups ($p<0.01$) and it was also significantly higher than the 50 mg/kg nanocurcumin group ($p<0.01$).

Conclusion: Nanocurcumin was able to reduce the activity of osteoclasts and increase the degree of regeneration. The expression levels of osteocalcin, Runx2 and osteoprotegerin increased significantly and dose-dependently under the effect of nanocurcumin. These findings indicate that it may be possible to use nanocurcumin as a drug for the prevention and treatment of osteoporosis in the future.

Keywords: Osteoporosis, Nanocurcumin, Ovariectomy

Exploring the Therapeutic Potential of Copper-Cysteamine Nanoparticles Combined with Cisplatin in Cervical Cancer Treatment (Research Paper)

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Introduction: The field of combination therapy involving nanoparticles and conventional chemotherapy has recently gained considerable attention for its potential to improve therapeutic outcomes. Copper-Cysteamine nanoparticles (Cu-Cy NPs) have emerged as a promising candidate for various medical applications in nanotechnology, including cancer therapy. These nanoparticles possess unique properties that make them effective in combination with other treatment modalities. This study aims to investigate the effects of Cu-Cy nanoparticles in combination with cisplatin, a widely used chemotherapeutic agent, on HeLa human cervical cancer cells. The findings from this research will provide considerable insights into the potential of Cu-Cy nanoparticles as a novel approach to enhance the efficiency of chemotherapy.

Methods: In this investigation, we evaluated the cytotoxicity effect of Cu-Cy nanoparticles and cisplatin in various concentrations on HeLa cancer cells, both individually and in combination. To ensure sublethal individual treatment doses, we selected the IC25 dose of cisplatin based on preliminary dose-response experiments. Additionally, we conducted experiments to assess the combined effects of these substances. Cell viability was quantitatively determined using the MTT assay, while apoptosis was assessed using Annexin-V/PI staining, followed by flow cytometry analysis. Cell migration was evaluated through a wound healing assay.

Results: Our findings revealed a significant reduction in cell viability, with the combination treatment resulting in a cell survival rate of 54.89%. In contrast, cisplatin monotherapy and Cu-Cy NPs alone exhibited cell survival rates of 73.5% and 93.85%, respectively. The calculated combination index (CI) of 1.06 suggested a closely additive interaction between the two agents. Additionally, apoptosis analysis showed a significant increase in the apoptotic cell population (36.82%) in the combination group, compared to nanoparticle monotherapy (6.05%) and cisplatin monotherapy (15.54%). Furthermore, the

combination treatment substantially inhibited cell migration compared to the control and other treatment groups.

Conclusion: In conclusion, our study highlights the potential of Cu-Cy NPs to enhance the therapeutic effectiveness of cisplatin in cancer treatment. The combination of Cu-Cy NPs with cisplatin resulted in a significant reduction in HeLa cell viability, exceeding the outcomes achieved with either agent alone. Moreover, the observed increase in apoptosis and inhibition of cell migration in the combination group further supports the potential clinical relevance of this approach. These findings underscore the importance of exploring nanoscale drug delivery systems in conjunction with conventional chemotherapy to maximize treatment outcomes. While our study provides major insights, further investigation is required to elucidate the underlying molecular mechanisms and validate the translational potential of Cu-Cy NPs in combination with cisplatin in preclinical and clinical settings. This research represents a step forward in the ongoing effort to develop more effective and targeted cancer therapies.

Keywords: Copper-Cysteamine nanoparticles, Cisplatin, Apoptosis, Migration, Cervical cancer.

Expression change of Multidrug Resistance Protein (MRP1) modulates chronic salinity tolerances of sea urchin Echinometra mathaei
(Research Paper)

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Introduction: The attainment of any organism relies on environmental plasticity and also on its aptitude to survive to ecological variation (for instance preserving homeostasis in stress conditions). The multidrug resistance protein (MRP) family encrypts a diverse repertoire of ATP-binding cassette (ABC) transporters with multiple roles in development, disease, and homeostasis. Understanding MRP evolution is significant to separating their roles in their miscellaneous actions. Sea urchins occupy an essential phylogenetic point for considering the evolution of vertebrate proteins and have been an imperative invertebrate model organism for study of ABC transporters. However, under non pathological conditions in mammals/sea urchins, MRP1 has been confirmed to perform several roles that comprise control of inflammatory response of mast cells. These tasks are apparently associated with the capacity of this protein to carry endogenous biomolecules that perform straightly or secondarily as signaling molecules. In general, sea urchins are considered a worthy taxa for biomonitoring researches because of its benthonic adult long-lasting life, hence straight exposed to anthropogenic pollutants. The coelomic fluid of the sea urchin comprises free immune effector cells, among them, red sphere cells, showed an excessive upsurge in quantity in individuals collected from contaminated environments. These cells activate their response strategy against diverse types of physical and chemical disturbances/pollutants/stressors. All these actions yield an increase in the content of the classical stress protein, such as heat shock protein 70 and transporters. Furthermore, their upregulation throughout cellular stress supports organism resistance during stressful situations and make them main effector of both defense and immune systems.

Methods: Individuals of E. mathaei were collected from the intertidal zone during the low tide from desalination plant discharge outlets, then coelomic fluid of each specimen (up to 2 mL) was withdrawn. For protein isolation, the coelomic fluid was centrifuged at 12,000g, for 20 min at 4 °C, and 15 µg of the

supernatant from control and salt stressed sea urchins was separated in a 12% SDS-PAGE gel. The 45 kDa band were selected for MALDI-TOF analyses. After tryptic digestion, the resultant peptide fragments were injected to a MALDI TOF/TOF Mass Spectrometer and the role of them was evaluated using homology analyses in reference to annotation of their homologs.

Results: In this study, SDS gel electrophoresis and matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF-MS) technology was used to examine differentially expressed proteins in coelomic fluid from control and salt stressed individuals of E. mathaei. SDS-PAGE proteins profile of CF extracts showed intense bands at 45 kDa. After the BLASTp searches against the NR database, the transcript sequences were further clustered according to the top hits found (E-value, 8E-15 to 1E 10). Consequently isoforms gave an identical primary structure in the protein matching and were classified as ATP-binding cassette transporters. Finally, BLASTp comparisons revealed the closest homologous sequence as multidrug resistance protein (MRP) with 87 % Query cover (EV, 1e-14).

Conclusion: The multidrug resistance protein (MRP) are a group of extremely conserved proteins, deciphered in vertebrates and invertebrates while they are exposed to cellular stress. The transporters are vital osmoregulation elements, responsible for the uptake and efflux of main materials such as mineral ions, sugars and amino acids. These proteins also play an important role in detoxification and chemo protection by transporting a wide range of compounds, especially conjugates of lipophilic substances with glutathione, glucuronate and sulfate. This protein was shown to have a molecular weight of 190 kDa, but he sea urchin MRP appears to have additional protein components in the molecular weight range of 14-55 kDa that might correspond to a cargo. Moreover, researchers have proved that sea star P-gp-like transporter are different from vertebrate P-gp transporters. They demonstrated that reactive MRP migrated at 45 kDa rather than in the 150–200 kDa range of vertebrate P-gp transporters in SDSPAGE. This study has shown that multidrug resistance protein expression level was higher in salt stressed sea urchins E. mathaei, and this indicating MRP transporters perform a pivotal role in responding to stress. In the white leg shrimp Litopenaeus vannamei, ABC transporters showed an essential task in the physiological fluctuations associated with uptake, tolerance, and cell detoxification when they were exposed to stress.

Keywords: ABC transporters, hyper salinity, tolerance, MALDI-TOF-MS, Echinometra mathaei.

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Fabrication and characteristics of chitosan nanofibrous mat coated by hyaluronic acid and resveratrol as a tissue engineering scaffold
(Research Paper)

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Introduction: The healing of wounded skin possesses intricate nature. Fabricating of scaffolds as wound dressing has been noticed in clinical applications. In the present study, we designed nanofiber mats of chitosan (CS) via electrospinning with subsequent coating by Hyaluronic acid (HA) and Resveratrol (RS) for their efficacy in immunoprotection and pro-angiogenic features respectively.

Methods: The developed nanofibrous mats were characterized by SEM, FTIR, TGA, tensile testing, in vitro release study and human dermal fibroblasts seeding assay.

Results: The results revealed that human dermal fibroblasts adhered and proliferated in all scaffolds and no significant cytotoxicity was observed. However, cells infiltrated deep into the scaffold were more detected in porous CS/HA and CS/HA/RS scaffolds compared to the CS scaffold. CS/HA nanofibers indicated more interactions between HA and CS. Water absorption measurement revealed differences in the wettability of resultant fibers. Although both scaffolds showed high wettability, the CS/HA/RS had lower wettability than CS/HA.

Conclusion: The present findings indicate that the fabricated electrospun CS/HA and CS/HA/RS scaffolds has excellent biomechanical properties and

may be a preferable candidate scaffold, since it can also effectively serve as a carrier of growth factors because of its structural, mechanical, and releasing properties.

Keywords: Chitosan, Hyaluronic acid, Electrospinning, Resveratrol, Nanofiber

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Fabrication and characterization of fresh Osteochondral scaffold for cartilage tissue engineering (Research Paper)

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Introduction: Regarding the worldwide undeniable privilege of Cartilaginous joint injuries and insufficient repairability of the native cartilage tissue in case of defect occurrence because of a lack of adequate blood vessels and nutrition delivery, achieving a suitable approach for cartilage regeneration has become challenging in the last decade. Benefiting from allograft fresh osteochondral scaffold which contains living cells may be presented as a novel method for the treatment of cartilage injuries, osteoarthritis, etc.

Methods: The methods of providing osteochondral tissue were carried out according to the guidelines of Euro GTP, AATB, ISO 13485 quality management system, and the requirements of the Medical Equipment Administration of Iran. In this procedure, donors between the ages of 15 and 40 were screened based on their medical history and serology tests to ensure a lack of any bioburden (such as bacteria, yeast, mold, etc.) or hazardous viruses (such as HIV, HCV, HTLV1, etc.). Osteochondral tissue was harvested from brain-dead donors in less than 6 hours and produced in a class B cleanroom under aseptic conditions in dimensions of 10 mm. The microstructure of the graft was observed by scanning electron microscopy (SEM). The osteochondral scaffold was evaluated for the survival of living cells by the DAPI staining until 28 days of processing.

Results: The serology as well as the bioburden assays demonstrated the absence of any risk-causing microorganisms. The resulted structure according to the SEM images seemed integral resembling an efficient osseocartilaginous tissue. Based on the obtained DAPI images, intact cell nuclei were observed on both bone and cartilage phases until 28 days after harvesting which could be evidence of the scaffold repairability due to cellular

proliferation and eventually cartilage regeneration in case of implanting in the defect.

Conclusion: Fabricating fresh osteochondral scaffold could be a promising procedure for ameliorating cartilaginous diseases due to its repairability which was evidenced in vitro.

Keywords: Allograft, Scaffold, Cartilage Regeneration, Fresh Osteochondral.

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Fabrication and cytotoxicity of surface-capped maghemite nanoparticles with oleic acid (Research Paper)

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Introduction: Maghemite (γ-Fe2O3) nanoparticles exhibit unique magnetic properties and the capacity to interact with biological molecules and cells at the cellular level, causing them to be a worthwhile choice for multiple biomedical purposes.

Methods: we synthesized maghemite NPs using ammonium hydroxide as a precipitating agent in the chemical co-precipitation method. Proper maghemite NPs size necessitates the appropriate reaction temperature and surface modification. Herein, oleic acid (OA) was utilized as a capping agent to enhance NPs properties.

Results: In this study, the maghemite nanoparticle size was effectively handled to be in the 16-27 nm range. An analysis of their structure and morphology was carried out by field-emission scanning electron microscopy (FE-SEM), energy dispersive X-ray spectroscopic (EDS), transmission electron microscopy (TEM), Fourier transforms infrared spectroscopy (FTIR), and X-ray diffraction (XRD). Moreover, the magnetic behavior was studied through a vibrating sample magnetometer (VSM). These NPs were then found to be superparamagnetic iron oxide NPs (SPIONs) with high saturation magnetization (36.5 emu/g). The in vitro cytotoxicity assessments on human cervical cancer (CaSki) and normal human umbilical vein endothelial (HUVEC) cells showed that NPs in neither cancer nor the normal cell lines were cytotoxic, even when dosed at 50 µg/mL.

Conclusion: The safety and size of capped-NPs with OA make them potentially valuable for further therapeutic and diagnostic in biomedicine.

Keywords: Maghemite, Superparamagnetism, Cytotoxicity, Biocompatible, Iron oxide.

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Fabrication of bilayer hydrogel wound dressings with using chitosan and polyvinyl alcohol and herbal compounds to enhance the healing effects of wound dressing (Research Paper)

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Introduction: In recent years, the development of bilayer wound dressings, which consist of two distinct layers with varying properties, has garnered significant attention in the field of wound care. These dressings hold great promise for addressing various aspects of wound management, including pain relief, inflammation reduction, and promoting the overall wound healing process. The primary objective of our research was to design and evaluate a bilayer hydrogel wound dressing by incorporating herbal compounds and biodegradable polymers. This innovative approach aims to enhance the efficiency of wound care procedures

Methods: To achieve this goal, we focused on the synthesis of the top layer of the wound dressing. We utilized key biomaterials, including a 2 wt% chitosan solution, a 0.5 wt% agar solution, and polyvinyl alcohol (PVA) solution. Our aim was to create three different specimens with various mass ratios of 0.5 wt% agar solution and PVA (20%, 25%, and 30% of each component), while maintaining a constant mass ratio of 50% for the 2 wt% chitosan solution. For the fabrication of non-fluid sublayers, we employed a combination of ingredients, including Ocimum basilicum mucilage, a 2.5 wt% agar solution, and a 9 wt% polyvinyl alcohol solution. These components allowed us to produce three different specimens of sublayers with distinct mass ratios, offering a range of properties and functionalities. To further enhance the therapeutic effects of wound dressing, we introduced curcumin into the sublayer specimens. Curcumin is a bioactive compound known for its anti-inflammatory and wound healing properties. We varied the concentration of curcumin in the sublayers to explore the optimal configuration for promoting wound healing. In our pursuit of creating an antibacterial wound dressing, we investigated the biosynthesis of silver nanoparticles. The green synthesis method was chosen to minimize the environmental impact and health concerns associated with chemical synthesis. Four different concentrations of silver nanoparticles (0.5 wt%, 1 wt%, 2 wt%, and 3 wt%) were incorporated

into the sublayer specimens, allowing us to evaluate their antibacterial properties against various microbial cultures.

Results: Our comprehensive evaluation of the bilayer wound dressing included assessments of curcumin delivery rates, the mechanical properties of the top layer specimens (such as tensile strength and Youngs modulus), antibacterial activity of silver nanoparticles against both gram-negative and gram-positive bacteria, nanoparticle characteristics through Dynamic Light Scattering (DLS) analysis, water absorption capabilities of the specimens, and the analysis of biopolymers, herbal compounds, and synthesized specimens through Fourier transform infrared spectroscopy (FTIR) and scanning calorimetry (DSC). Our findings revealed that sublayer specimens with higher agar content and lower mucilage content demonstrated the highest curcumin release rates, aligning with our goal of efficient wound healing. Tensile strength tests demonstrated that an increased mass ratio of PVA in the top layer specimens improved the mechanical properties, attributed to elastic characteristics of PVA. The antibacterial assessments were notable, showing that silver nanoparticles had stronger antibacterial effects on microbial cultures containing gram-negative bacteria, such as Escherichia coli, compared to cultures with gram-positive bacteria, such as Staphylococcus aureus. Furthermore, the concentration of silver nanoparticles in sublayer specimens had a significant impact on their inhibitory effects against gram-negative bacteria. Dynamic Light Scattering analysis of the nanoparticles revealed a spherical morphology and uniform dispersion, while the water absorption tests indicated that the percentage of water absorption increased with a higher mass ratio of agar in the sublayer specimens. FTIR analysis confirmed the presence of functional groups of chitosan, curcumin, PVA, agar, and silver nanoparticles in both top layers and sublayers. Lastly, DSC analysis provided insights into the thermal resistance of the sublayer specimens, with increased mass ratios of agar solution and mucilage correlating with improved thermal stability.

Conclusion: In conclusion, our research has successfully developed a bilayer wound dressing that exhibits promising potential in wound care. This dressing offers efficient curcumin delivery, improved mechanical properties, strong antibacterial effects, and noteworthy nanoparticle characteristics. It holds the potential to enhance wound healing processes and revolutionize wound care practices.

Keywords: Hydrogel wound dressing, Curcumin, Ocimum basilicum mucilage, PVA, Chitosan

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Fabrication of PES scaffold coated by leech saliva for vascular tissue engineering (Research Paper)

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Introduction: Leech saliva has lots of effective components reported previously. Some of the important proteins in leech saliva are Hirudin, Destabilase, Factor Xa inhibitor, Antistasin, Hyaluronidase, and Collagenase. It has anti-inflammatory and analgesic properties, inhibits C1 complement, permits diffusive distribution, improves blood flow, and inhibits platelet adherence. Cardiovascular diseases can be treated with it as a drug according to studies. An artificial blood vessel must contain both the structure and mechanical properties of a real blood vessel. Accordingly, polyether sulfone electrospun fibers were used in this project. Polyether sulfone is a biomaterial extensively utilized in haemodialysis membrane production, owing to its remarkable chemical and mechanical properties.

Methods: The scaffold concentration was 30%, Followed by an electrospinning feed rate of 0.5mL/h, voltage 20kV, and collection distance of 25 cm. To prepare leech saliva, a nauseating solution was prepared by combining sodium chloride and arginine. After feeding the leeches with solution, the leeches were placed in ice and they vomited. Prepared saliva was centrifuged. Different concentrations of 2.5%, 5%, and 7% of protein solution were prepared. Oxygen plasma was used to activate the surface of the scaffolds for coating. Then, the scaffolds were placed in an EDC/NHS solution. Afterward, they were placed in protein solutions.

Results: The concentration of protein solution and constituent proteins were determined using the Bradford and SDS-PAGE method. The concentration of protein was 1.9665±0.053mg⁄ml. The morphologies of the materials were observed via SEM. The obtained fibers were uniform. The average fiber diameter was 0.507±0.136µm and the percentage of porosity calculated was 49.041%. The chemical structure was characterized using ATRI spectroscopy. To verify the developed coating, SEM imaging and ATRI assessments were conducted, and the resulting peaks validated the surface alteration and establishment of a protein coating. Surface wettability was tested with a water contact angle instrument. It was clear that the contact

angle of the surface with water decreased with the increase of concentration in the coated protein, which indicated the increase in the hydrophilicity of the fibers. A tensile test was used to check the mechanical properties of the scaffold. Its Young's modulus was 1.40MPa, which is similar to normal coronary arteries, ultimate strength was 3.44MPa, and ultimate strain was 4.39. Anticoagulants in leeches destroy coagulation factors 2 and 10. Considering that coagulation factor 2 is in both the intrinsic and extrinsic pathways, it was expected that a change would be observed in both APTT and PT times. PT and APTT times increased with increasing protein concentration and increased blood compatibility and anticoagulation of the scaffolds were confirmed. To check the antihaemolytic of the scaffolds, Na and K ions, and LDH enzyme were checked. The obtained data didn't show any hemolysis. MTT test was performed on HUASMC on day 3 and HUVEC on days 1, 3, and 7 and DAPI staining was performed on HUVEC on day 3 to check biocompatibility. Regarding the use of scaffolds for vascular, it is expected to increase the growth and proliferation of the HUVEC and decrease the growth and proliferation of HUASMC with an increase in the concentration of the scaffold coating. An increase in cell growth and viability of HUVEC was observed with increasing coating concentration. Notice that, by increasing the concentration from 5% to 7%, the rate of cell growth and proliferation decreased. This is due to the presence of the hirudin protein, which prevents any sticking to the surface from a certain concentration, which is the property of all anticoagulants that occur from a certain concentration. This shows that the optimal concentration is 5%. As expected, cell growth and viability of HUASMC decreased with increasing concentration. On the third day, DAPI staining was conducted on HUVEC, confirming the findings of the MTT test. According to staining, the number of cells increased from 2.5% to 5% and decreased from 5% to 7%.

Conclusion: In this study, we developed vascular tissue engineering scaffolds via electrospinning PES coated by leech saliva. These scaffolds promoted HUVEC growth and suppressed HUASMC proliferation. Furthermore, these scaffolds displayed excellent blood compatibility via a prolonged blood clotting time. In summary, PES scaffolds coated with leech saliva hold potential applications in vascular tissue engineering due to efficient endothelialization and decreased SMC proliferation.

Keywords: leech saliva, vascular tissue engineering, HUASMC, HUVEC

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Fecal microbiota transplant as a potential treatment for Alzheimer's disease (AD) (Review)

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder that affects millions of people worldwide and can lead to cognitive impairment and progressive memory loss. The disease is characterized by the accumulation of tau-protein and β-amyloid plaques in the central nervous system (CNS), which affect neurons in the cortex of the brain, especially the hippocampus. AD worsens memory and can lead to people becoming unable to function independently in society. Given that AD is associated with abnormal gut microbiota, microbiota-targeted interventions such as fecal microbiota transplantation (FMT) might represent a potentially attractive therapeutic option against AD. The purpose of this study was to evaluate the significance of fecal microbiota transplantation (FMT) as a potential therapeutic option against Alzheimer's disease (AD).

Methods: Our study was conducted on the PubMed database using the keywords "Fecal Microbiota Transplantation" and "Alzheimer Disease" since 2020. Out of 25 papers related to this topic, 15 were reviewed.

Results: Some previous studies have shown that the pathogenesis of Alzheimer's disease (AD) is associated with the gut microbiome through the brain-gut axis. The imbalance of intestinal flora can stimulate microglia as cells of innate immunity and cause the secretion of pro-inflammatory cytokines. Additionally, short-chain fatty acids as metabolites of intestinal flora could regulate the synthesis of hormones. Therefore, microbiota-mediated intestinal and systemic immune aberrations and alteration in peripheral circulating hormones contribute to the pathogenesis of AD. Furthermore, The bacterial community and genetic background might be correlated to AD severity and progression. These findings provide a novel framework for understanding the role of gut microbiota in AD. Findings have suggested that FMT seems a possible treatment route because it could improve cognitive function in AD by glial reactivation, slowing Aβ plaque deposition, recovering synaptic dysfunction and neuroinflammation, and decreasing the tau-protein.

Conclusion: The protective effects of FMT may be related to reversing alterations of gut microbiota and its metabolites. However, more research in this area may lead to both novel treatments and a better understanding of the mechanisms behind Alzheimer's disease.

Keywords: FMT Microbiota Alzheimer

Fenitrothion biodegradation by bacterial tools (Review)

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1.
2.

Introduction: The development of agriculture and the widespread use of various insecticides have resulted in extensive contamination of drinking water sources used by humans. One solution to prevent the spread of contamination is the degradation of these insecticides within the soil environment before they reach drinking water supply. Certain bacteria possess the ability to degrade various types of insecticides, and in this context, we present an overview of some bacteria that impact fenitrothion biodegradation, a widely used insecticide found in different locations

Methods: Organophosphorus insecticides such as fenitrothion (with the chemical formula: O, O-dimethyl O-p-nitro-m-tolyl phosphorothioate) are used to control various populations of insects. .1 In natural conditions Fenitrothion, as an organic poison is a yellow-brown liquid with a distinct smell. Fenitrothion enters the market with different formulations (7). Because of its limited solubility in water, fenitrothion exhibits low penetration into underground water. However, its binding to the soil is relatively robust, and depending on the level of aeration, it can remain in the soil and even in water for weeks to months.

Results: Very small amounts of it evaporate and degrade in the atmosphere within a few days to a few weeks. therefore, its global environmental effects cannot be ignored. Unfortunately, Fenitrothion emulsion has the ability to accumulate in aquatic organisms and shows good stability in hard water.2 bacterial degradation has been reported as one of the strategies for the detoxification of the insecticides in green way. While many of them isolated and characterized as co-metabolically hydrolyzing organophosphorus insecticides only some species that utilize an insecticide as a sole source of carbon and energy for growth have been reported. Burkholderia sp. NF100 Strain and two plasmids- pNF1 and pNF2- which isolated from fenitrothion-treated soil show the degradation ability. 1 The NF100 strain was found to initially hydrolyze the organophosphate bond of fenitrothion, resulting in the formation of 3-methyl-4-nitrophenol as an intermediate product. This compound subsequently led to the production of methylhydroquinone as the final product of the degradation process. 1 the other bacteria have been reported is Burkholderia sp. FDS-1 which isolated from the sludge of the

wastewater treating system of one of organophosphorus pesticides manufacturers. Burkholderia sp. FDS-1 is a gram-negative bacterium with a short rod shape and has the same function as sp. Strain NF100 in metabolization. Therefore, its final products are nitrite and methylhydroquinone. The report declares that there would be little effect on fenitrothion hydrolysis by adding other carbon sources and omitting the phosphorus source.3 The other reported bacteria from Burkholderia species are sp. strain YI23 which isolated from a golf course soil and identified as a fenitrothion-degrading bacterium. sp. strain YI23 genome consists of three chromosomes and three plasmids And the degradative gene's locations are on plasmids BYI23_E and BYI23_F.4 Bacillus subtilis PCI 219, isolated from pine forest soil, is another Fenitrothion degrader reported by MIYAMOTO et al.5 Other reports have mentioned that the B. stearothermophilus strain AG-49, in conjunction with silica, was used in a mineral medium for the degradation process. These reports indicated a 5% degradation within a span of four days6 Ghafari et al reports about Pseudomonas aeruginosa strain F4, Pseudomonas fluorescens strain F1 and Bacillus cereus strain F3 isolation which have collected from pistachio gardens. they present that Pseudomonas aeruginosa strain F4 has shown the best result. 2

Conclusion: Various bacteria have been investigated for the degradation of agricultural Pesticides in different environments and different soil ecosystems, and it has been shown that different species of bacteria have the ability to degrade agricultural Pesticides. Due to the widespread use of fenitrothion throughout our world We have to control its spread in soil and water environments. The research process is still needed for the proper use of this category of microorganisms in order to know more about the metabolic pathways and effective genes. 1)doi: 10.1128/aem.66.4.1737-1740.2000 2)Isolation and characterization of Fenitrothion-degrading bacteria from pestachio gardens in Kerman Provinance Mehrnosh Ghafari 1 Mehdi Hassanshahian 2 Mohammad Mahani 3)Isolation of fenitrothion-degrading strain Burkholderia sp. FDS-1 and cloning of mpd gene DOI 10.1007/s10532-005-7130-2 4)Complete Genome Sequence of the Fenitrothion-Degrading Burkholderia sp. Strain YI23 DOI: https://doi.org/10.1128/jb.06479-11 5)Degradation of Fenitrothion by Bacteria Isolated from Forest Soil - Yoko SATO 6)Degradation of fenitrothion byBacillus stearothermophilus adhering to silica https://doi.org/10.1007/BF02815535 Australian Pesticides and Veterinary Medicines Authority (APVMA). The reconsideration of approvals of the active constituent fenitrothion, registrations of products containing fenitrothion and their associated labels 2004; 9-50.

Keywords: fenitrothion- insecticides- biodegradation

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Fluoxetine Induces Oxidative Stress Dependent DNA Damage in Human Hepatoma Cells (Research Paper)

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Introduction: Fluoxetine is a selective serotonin reuptake inhibitor is a commonly used drug for the treatment of major depression (MD). Despite the positive effects of this drug it seems to be associated with various side effects. Genotoxicity or DNA damage is an important side effect of different drugs in different categories. However, to date, the genotoxicity and cytotoxicity of Fluoxetine are partially unknown

Methods: In the present study ROS, MDA and GSH evaluation methods were used for oxidative stress detection in HepG2 cells treated with Fluoxetine (1-10µM). Comet assay tried to evaluate the genotoxic effects of Fluoxetine and Flow cytometry was also used to apoptosis detection in these hepatic cells

Results: Our data showed that 1h after treatment with Fluoxetine the MDA and intracellular concentration of ROS was increased significantly in a concentration-dependent manner ($p<0.001$).While the amount of GSH was reduced also significantly ($p<0.001$). Our results also clearly indicated that Fluoxetine treatment resulted in the increased DNA damage of HepG2 cells. Tail percentage of DNA for control cells was 4% but this percentage was 19%, 28% and 32% for 1, 5 and 10 µM of Fluoxetine, respectively ($P<0.01$ and $P<0.001$). Our data of flow cytometry also showed increasing the early and late apoptosis to 13.31% and 9.54%, respectively. In the concentration of 5 µM, the percentage of cells in early apoptosis was 40.25% and 40.52% in late apoptosis. Another concentration of Fluoxetine (10 µM) led to catastrophically increasing the early and late apoptosis to 25.49% and 48.75%, respectively

Conclusion: In conclusion, the present study showed that Fluoxetine is able to oxidative stress-dependent damage DNA. Therefore, due to the high incidence of depression, the genotoxic effects of Fluoxetine should be emphasized. However further study is needed to confirm our study.

Keywords: Fluoxetine, Genotoxicity, DNA damage, Depression, ROS, Apoptosis

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Focused Ultrasound and Nano-bubbles can induce the permeability of Neuroblastoma cells (Research Paper)

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Introduction: By combining focused ultrasound application with nano-bubble system, we assume to induce the permeability of biological barriers and so, allowing drugs to enter the targeted part of a tissue. This occurs when nano-bubbles exert mechanical stresses on the vessel walls by oscillating. So far, the long ultrasound pulses have been employed regarding some preclinical and clinical cases. The purpose of this study is to optimize in vitro sonoporation through characterization of the effects of nano-bubble on tissue permeabilization rate. After fabrication and characterization of 100 nm lipid nano-bubbles, their effects under therapeutic ultrasound on sonoporation in the cells, utilizing fluorescein isothiocyanate (FITC) dextran (70 kDa) as fluorophore marker are verified.

Methods: We applied ultrasound pulses (1 MHz, 10% duty cycle, 2.0 W/cm2 at 100 Hz pulse repetition frequency) onto the cells. Nano-bubbles containing FITC-Dex, as a probe, was administered before application of ultrasound pulses. Cells were extracted after 0, 10 or 20 seconds of the ultrasound treatment to assess the extent of FITC. Triton X-100 (TX100) was used during an experimental period of 30 minutes. The cells underwent irreversible permeabilization of the membrane and structural collapse. The permeability of cell could determine with the aid of the scan methods in spectrofluorometry.

Results: Brightfield and fluorescence nanoscopy of sonoporated cells showed obvious internalization of the FITC-dextran. The control sample, which was exposed to nano-bubbles and FITC-dextran without insonation, showed little or no residual FITC-dextran on the cell surfaces. Fluorescence intensity of sonoporated cells was statistically different from those unsonoporated with bubbles at all concentrations, while the fluorescence

intensity of cells sonoporated with the bubbles was not statistically different at variant concentrations.

Conclusion: The results of this study indicate that nano-bubble concentration does not interact dynamically to affect sonoporation efficiency. With respect to the role of nano-bubbles for sonoporation of suspended cells, the additional control over drug-delivery and improvement in drug-uptake is promising.

Keywords: Drug Delivery; Focused Ultrasound; Nanotechnologies.

FODMAP diet: is it effective on IBD or just overrated? (Review)

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Introduction: IBD is an umbrella under which there are several intestinal conditions including Crohn's Disease(CD), Ulcer Colitis(UC), and pouchitis abbreviated as IBD intestinal disease which cause severe inflammation, ulcers, and other structural damage. People with IBD and IBS are a large group of people who can be defined as 30-50% of patients going for gastrointestinal(GI) services or up to 25% of adults in the United States. Nowadays, pharmacological treatment is the first step of treatment. antibiotics like Rifaximin are recommended for this patient but this treatment can lead to other problems related to using antibiotics. Due to this reason, other ways that can reduce using antibiotics can help to decrease the rate of problems that resulted from using antibiotics. some diet like the low-FODMAP diet(LFD) has been shown to ameliorate FGS (functional gastrointestinal symptoms) by reducing diet-induced luminaire water, colonic gas, and, consequently, luminaire distension-induced visceral hypersensitivity. In this study, we aimed to assess the effect and safety of a low-FODMAP diet by assessing clinical and biochemical disease activity, and quality of life(QOL) in patients with IBD.

Methods: This is a review study that was gathered by searching keywords, IBD, Inflammatory bowel disease, and FODMAP diet in google scholar, and PubMed. After these articles were reviewed, a general conclusion was extracted from all the articles. this review was written by merging the summary of all data based on searching.

Results: This study reviewed 8 related studies that revealed the effect of the low-FODMAP diet. Studies indicate that the low-FODMAP can improve GI and FGS symptoms. The IBS-like symptoms were not present in 66.1% of patients after 6 weeks on LFD. LFD affected patients with ulcer colitis (59.3%) and Crohn's disease (71.9%). If we compared the patients on an LFD to those on a normal diet(ND), we understood that LFD reduced pain duration and degree of pain as well as improved in stood frequency. IBS-SSS is the score of pain, bloating/distension, and IBS-related quality of life(QOL) measured by CRP. This measurement showed that patients experiencing CRP remission had a response in both the LFD and ND groups but with a larger response in

the LFD group. IBD-GOL did not improve in either the LFD or ND. This diet is also compared to the sham diet the diet that is eaten but not digested or absorbed. In UC, there was a greater reduction in IBS-SSS score following LFD. But in CD, both were equally effective in the reduction of IBS-SSS score. To sum up, LFD can relieve FGs in 56% of patients with IBD in a retrospective study and 78% of IBD patients in a prospective study.

Conclusion: According to the above, a low-FODMAP diet proved to moderate the symptoms of IBD. It provides sufferers with a better quality of life. According to the conducted studies, no definite conclusion can be made. The number of studies has not been enough. So more research needs to be done and then we can discuss clearly its effects.

Keywords: IBD, Inflammatory bowel disease, FODMAP

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Free Radical Scavenging Activity of Collagens/Collagen Hydrolysates from the Swim Bladder of Caspian kutum (Research Paper)

Rezvan Mousavi Nadushan,[1,*] Maede Hosseini,[2]

1.
2.

Introduction: Collagen is an extracellular matrix macromolecule (~300 kDa), constituted of three α peptide chains with a triple-helix construction and repetitive proline-rich Gly-X-Y sequences where X and Y most commonly represent proline and hydroxyproline, respectively. Collagen and its derivatives have been extensively applied in the food, cosmetics, medicine and pharmaceutical industries and the total demand from all over the world for collagen has amplified over the years. Collagen has excellent biocompatibility, limited immunogenicity, high antioxidant activity and coagulation function, and is considered a promising biomimetic scaffold. Normally, the content of type I collagen in the skin of babies and youngsters is negatively associated with age. After middle age, dermal fibroblasts function and collagen synthesize diminish annually; meanwhile, the firmness and constancy of collagen filaments intensify.

Methods: Acid-soluble, Pepsin-Soluble Collagen and Collagen Hydrolysate Preparation Fresh swim bladder of Caspian white fish Caspian kutum was carefully cleaned and the unnecessary tissue was removed. The swim bladder was cut into small pieces. Swim bladder samples were extracted by acetic acid and pepsin, then again acid soluble collagen (ASC) and pepsin soluble collagen (PSC) were hydrolyzed enzymatically (by pepsin). DPPH radical scavenging activity The hydroxyl radical scavenging activity was determined by using DPPH (0.2%) in ethanol. The absorbance of the mixture was determined at 517 nm (As).The sample replaced with deionized water was set as the control group (Ac), and the DPPH exchanged with ethanol was established as the blank group (Ab). The DPPH radical scavenging activity of the samples was calculated as follows: PPH radical scavenging activity (%) = [1- (As-Ab)]/Ac × 100%

Results: All samples including (ASC), (PSC), (ASCH), and (PSCH) had a DPPH radical scavenging activity superior to 50%. The highest scavenging activity (81.4%) was for (PSCH, Pepsin Soluble Collagen Hydrolysate).

Conclusion: Nowadays, marine collagen or collagen active peptides have attracted broad attention in pharmaceutical, cosmeceutical and skin care

industry due to their antioxidative, and anti-aging activities. During skin aging, it is desirable to neutralize ROS, which are implicated in skin damage. So the radical scavenging activity is a significant property for the cosmeceutical products expected at the inhibition of photaging and skin damage against UV radiation. At a distinct low concentration, the radical scavenging activity of PSC was higher than that of ASC, and the radical scavenging activity of (PSCH) was highest. The highest scavenging activity (81.4 %) for (PSCH) was superior to those reported for peptide fractions of Carp Fish Byproduct ranging from 61.8, 65.9, 72.7 attributed to >30 kDa, 10-30 kDa and 3-10 kDa. But the highest scavenging activity (81.4%) for (PSCH) from Caspian White Fish was close but lower than (87%) for <3 kDa at 1 mg/mL, for common carp. Once more, our findings for PSC hydrolysate but not peptide fraction, were superior to those obtained with byproducts of different fish species (maximum $DPPH^{\cdot}$ scavenging activity of 81% for <3 kDa fraction at 5 mg/mL) also were superior to 71.15% DPPH scavenging activity obtained with polypeptide fraction (molecular weight of 3 kDa) from swim bladder of Acipenser schrencki. In general, the worthy results attained could be associated with the existence of electron/hydrogen-donor polypeptides in the PSCH from swim bladder of Caspian White Fish, which interrupt radical chain reactions thanks to their proficiency to rejoin with free radicals.

Keywords: Caspian kutum , Swim Bladder, Collagen, Collagen Hydrolysate, Antioxidant.

Frequency of symptoms, clinical and paraclinical findings in dialysis patients with covid-19 (Research Paper)

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Introduction: In 2019, covid-19 emerged as a virus targeted respiratory tract and led to the acute respiratory distress syndrome and death. Several risk factors have been recognized for this virus and one of the important ones is dialysis. Covid-19 is common among patients undergoing chronic dialysis and its mortality is exceeding beyond 20%. In this study, we aimed to investigate symptoms, clinical and paraclinical parameters among dialysis patients infected with covid-19 in Kashan, Iran.

Methods: This was a cross sectional study conducted on 67 dialysis patients from February 2020 until August 2020. A questionnaire with demographic information including underlying diseases and dialysis condition, symptoms, clinical and paraclinical parameters was completed for each patient. Patients whose infection with covid-19 was confirmed by PCR test included in this study and those who had an incomplete questionnaire were excluded from the study. Data were imported in SPSS version 21 and descriptive parameters such as mode, mean, median, and SD along with inferential parameters were analyzed.

Results: Among 67 patients, 40 were men and the rest(27) were women. The mean age was 60 years old. Among participants, 9(13.4%) were admitted to ICU and 19(28.4%) were died. The most common comorbidities were hypertension(79.1%), diabetes mellitus(55.2%), and cardiovascular diseases (25.4%), respectively. Exertional dyspnea(71.6%), fever(61.2%), myalgia(61.2%), and at rest dyspnea(52.2%) were the most common symptoms among these patients, respectively. In CT-scan findings, 73.1% of patients had unilateral lung involvement. Collectively, these results indicated that admission in ICU, hypertension, intubation, cardiovascular disease

history, respiratory rate, lung involvement, SPO2, platelet count, CRP, and LDH had significant relationship with the patients outcome ($p<0.05$). Among these factors admission in ICU and intubation had stronger relation to final outcome of the patients as all(100%, $p<0.001$) of the patients admitted to ICU and 92.1($p<0.001$) of patients who were intubated were died. Death rate among patients who were not admitted to ICU and who were not intubated were 17.2 and 11.3%, respectively. Furthermore, Reduction of one percent in SPO2 could increase the chance of death by 16.5%. Additionally, SPO2 and intubation could change patient prognosis about 45.7% to 65.6%.

Conclusion: Taken all together, ICU admission, intubation and SPO2 had strong relationship to the patient prognosis as the change of these parameters especially SPO2 and intubation could change prognosis more significantly.

Keywords: hemodialysis, covid-19, paraclinical findings, symptoms

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From Matrix to Enamel: Exploring MMP20 and its Molecular Pathways in Human Tooth Development (Review)

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Introduction: The role of matrix metalloproteinase 20 (MMP20) in tooth development and enamel mineralization has been extensively studied. This review explores the significant role of MMP20 in human teeth and highlights the design of inhibitors targeting MMP20 as a potential therapeutic approach. Understanding the molecular interactions and mechanisms of MMP20 inhibition opens up new possibilities for dental research and clinical applications.

Methods: A comprehensive literature search was conducted using databases such as PubMed and Web of Science to identify relevant studies. Articles focusing on the role of MMP20 in tooth development, enamel mineralization, and the design of inhibitors were selected and thoroughly reviewed. The selected studies formed the basis for the exploration of the design strategies for MMP20 inhibitors in this review.

Results: Through the analysis of the available literature, it has been established that MMP20 is primarily expressed in enamel-forming cells known as ameloblasts. This enzyme is responsible for the proteolytic degradation of enamel matrix proteins, including amelogenin, ameloblastin, and enamelin, which are essential for proper enamel development. MMP20 activity is tightly regulated and influenced by factors such as pH, proteolytic inhibitors, and other molecules involved in the enamel formation process. The studies analyzed in this review demonstrate that MMP20 plays a critical role in enamel matrix degradation during tooth development. The dysregulation of MMP20 activity has been associated with enamel defects and dental pathologies. Consequently, the design of MMP20 inhibitors has gained attention as a potential therapeutic approach. Promising strategies for inhibitor design include small molecule inhibitors, peptide-based inhibitors, and natural compounds derived from medicinal plants, which have shown inhibitory effects on MMP20 activity.

Conclusion: The design of MMP20 inhibitors presents a promising avenue for dental research and clinical applications. By targeting the activity of

MMP20, these inhibitors have the potential to preserve enamel integrity and prevent enamel degradation. Additionally, the design of specific inhibitors may offer new insights into the underlying molecular mechanisms of MMP20 activity and its regulation during tooth development. Further research is needed to optimize the design of MMP20 inhibitors, considering factors such as specificity, stability, and delivery systems, in order to maximize their therapeutic potential. MMP20 regulates the biomineralization process by modulating the activities of other enamel matrix proteins. Additionally, MMP20 interacts with various signaling pathways involved in tooth development, including the Wnt and TGF-β signaling pathways. In conclusion, this review emphasizes the crucial role of MMP20 in tooth development and enamel mineralization. The design of inhibitors targeting MMP20 holds promise for dental research and clinical applications. Understanding the molecular interactions and mechanisms of MMP20 inhibition will contribute to the development of effective therapeutic strategies for the prevention and treatment of enamel defects and dental pathologies. Continued research in this area will further our understanding of the complex processes involved in tooth development and pave the way for innovative approaches in dental care.

Keywords: Matrix metalloproteinase 20, enamel mineralization, tooth development, ameloblast

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Fully automated segmentation of brain tumors from MRI images using convolutional neural network based on genetic and artificial bee colony algorithms (Research Paper)

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Introduction: Brain tumors are abnormal accumulations of cells in the brain, categorized as cancerous or non-cancerous. The conventional diagnosis involves visually analyzing magnetic resonance images (MRI), a time-consuming and error-prone process. This study introduces an automated brain tumor diagnosis system that integrates a genetic algorithm (GA), artificial bee colony (ABC) algorithm, and convolutional neural network (CNN). These components facilitate pre-processing, feature extraction, feature selection, and tumor area segmentation. Additionally, the proposed system quantifies the brain tumor area. Notably, the system achieves a sensitivity of 0.9721 and specificity of 0.9743, indicating its potential superiority in comparison to recent research findings.

Methods: The automated brain tumor diagnosis system integrates a genetic algorithm (GA), artificial bee colony (ABC) algorithm, and convolutional neural network (CNN). The GA is employed for pre-processing, extracting high-quality features from the images. Subsequently, the ABC algorithm assists in selecting the most pertinent features within a short timeframe. The CNN is then employed to conduct comprehensive analysis, precluding the need for manual intervention. The system is calibrated and validated against a dataset comprising more than 3000 MRI images.

Results: The developed automated brain tumor diagnosis system showcases commendable performance. It effectively integrates the genetic algorithm, artificial bee colony algorithm, and convolutional neural network for accurate pre-processing, feature extraction, and segmentation of tumor areas. The system's accuracy is evidenced by achieving a sensitivity of 0.9721 and a specificity of 0.9743. These outcomes signify a significant advancement, aligning with or surpassing the outcomes of recent research efforts.

Conclusion: In conclusion, this study presents an innovative solution to the challenges associated with brain tumor diagnosis. By leveraging the synergy of genetic algorithm, artificial bee colony algorithm, and convolutional neural network, the proposed system achieves substantial automation in pre-

processing, feature extraction, feature selection, and tumor area segmentation. The system's notable performance, with a sensitivity of 0.9721 and a specificity of 0.9743, underscores its potential to outperform existing methods. This research has implications for enhancing the accuracy and efficiency of brain tumor diagnosis, benefiting both medical professionals and patients.

Keywords: Brain Tumors, Segmentation, Convolutional Neural Network, Genetic, Artificial Bee Colony

Function of Efflux Pumps in Gram-Negative Bacteria (Review)

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Introduction: As indicated by recent kinetic modeling studies and experiments, the interplay between slow uptake and active efflux appears to be finely tuned. Therefore, even small changes in one or both factors can dramatically increase intracellular drug concentrations, rendering the bacteria susceptible to antibiotic treatment. This results in various possible approaches such as (i) the optimization of drugs for better influx and/or efflux avoidance, (ii) the permeabilization of the OM by additional chemosensitizers, or (iii) the inhibition of multidrug efflux pumps. Synergistic approaches between (ii) membrane permeabilizers and (iii) efflux pump inhibitors (EPIs) can also be used to sensitize Gram-negative bacteria to antibiotics.

Methods: In addition to possible acquired resistance mechanisms, Gram-negative bacteria already have a high intrinsic resistance to most clinical antibiotics, a property that can essentially be attributed to the combination of an additional outer membrane (OM) and the presence of powerful multidrug efflux pumps. The highly asymmetric OM of Gram-negative bacteria, which is formed by lipopolysaccharides (LPS) on the outer leaflet and phospholipids on its inner leaflet, represents a significant permeability barrier, particularly for hydrophobic compounds such as bile salts, disinfectants, and most antimicrobials. Consequently, the OM reduces the uptake of antibiotics. However, as a passive barrier alone, it cannot influence the resulting intracellular equilibrium concentrations. Multidrug efflux transporters actively counteract influx across the outer (and inner) membrane. As a result, many antibiotics reach only sublethal concentrations at their sites of action within the bacterium. Not surprisingly, multidrug efflux pumps have been found overexpressed in many clinical isolates.

Results: Efflux pumps are bacterial transport proteins which are involved in extrusion of substrates from the cellular interior to the external environment. These substrates are often antibiotics, imparting the efflux pump expressing bacteria antibiotic resistant phenotype. From the first drug-resistant efflux pump discovered in the 1990s, the development in molecular microbiology has led to the characterization of many efflux pumps in Gram-positive bacteria (GPB) including methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pneumoniae, Clostridium difficile, Enterococcus spp. and

Listeria monocytogenes and Gram-negative bacteria (GNB) such as cinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Stenotrophomonas altophilia, Campylobacter jejuni, Pseudomonas aeruginosa, Neisseria gonorrhoeae, Vibrio cholerae and Salmonella spp. Since these transport substrates against a concentration gradient, these efflux pumps are energy dependent. Based on the mechanism by which these derive this energy, the efflux pumps are broadly classified into two categories. The primary efflux pumps draw energy from active hydrolysis of ATP, whereas the secondary efflux pumps draw energy from chemical gradients formed by either protons or ions such as sodium. Efflux pumps have been categorized into five superfamilies, include (i) the ATP-binding cassette (ABC) family, (ii) the small multidrug resistance family, (iii) the major facilitator superfamily, (iv) the resistance-nodulation-division (RND) family, and (v) the multidrug and toxic compound extrusion family.

Conclusion: Here we give a brief explanation about RND. Members of the tripartite Resistance Nodulation cell Division (RND) superfamily are the major multidrug efflux pumps in Gram-negative bacteria. Tripartite RND efflux pumps consist of membrane fusion proteins (MFPs, also known as periplasmic adaptor proteins, PAPs), an RND core component, and an outer membrane factor (OMF), which together form an elongated complex that connects both the inner and outer bacterial membrane. The RND core component is present in the inner membrane (IM) as a homo- or heterotrimer. RND proteins recognize drug substrates and energize the drug efflux at the expense of the proton motive force (PMF). The MFPs build a hexameric ring on top of the RND proteins. In the active complex, this MFP forms a tubular structure, which connects to the open OMF porin in the outer membrane. As a result, substrates can be taken up by the RND core from the periplasm (or the outer leaflet of the IM) and removed from the cell by extrusion through the long MFP-OMF conduit across the OM. Some pathogenic Gram-negative bacteria contain multiple clinically relevant tripartite RND efflux pumps with partially overlapping substrate specificities such as MexAB-OprM, MexCD-OprJ, MexEF-OprN, and MexXY-OprM from Pseudomonas aeruginosa or AdeABC, AdeFGH, and AdeIJK from Acinetobacter baumannii that are either constitutively expressed (MexAB and AdeIJK), induced by stress, or overexpressed due to mutation. In other Gram-negatives such as Escherichia coli (AcrAB-TolC), Salmonella enterica (AcrAB-TolC), Klebsiella pneumoniae (AcrAB-TolC), Campylobacter spp. (CmeABC), and Neisseria gonorrhoeae (MtrCDE), single RND-tripartite systems appear to be dominant. It is critical that we look for novel strategies to combat the threat of antibacterial resistance. One potential strategy is to target the regulation of bacterial resistance mechanisms and another strategy is to target the regulation of gene expression.

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Keywords: efflux pump - Gram-negative bacteria - antibiotic resistant

Functional roles of long-noncoding RNA MALAT1 in breast cancer (Review)

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Introduction: Introduction: Breast cancer (BC) is the second most prevalent malignancy in women, which has been increasing worldwide. The two invasive types of breast cancer based on histology are invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), that IDC accounts for roughly 70 to 80 percent of all cases and a major cause of cancer-related death in women globally. Although recent studies investigated that over expression of MALAT1 has been implicated in the carcinogenesis of various cancers including BC, understanding functional roles of MALAT1 in breast cancer is crucial for developing targeted therapies that can disrupt its activities and improve treatment outcomes for patients with this challenging disease. Beside 2% of genome which is coded to protein, more than 98% of human genome is transcribed into ncRNAs. LncRNAs are a class of ncRNA which are defined as RNAs longer than 200 nucleotides that are not translated into functional proteins. LncRNAs have crucial roles in part of the epigenetic regulatory network, transcription and post-transcriptional regulation. Among the numerous lncRNAs that have been associated with various malignancies of multiple organs, including breast, the long non-coding RNA Metastasis-associated lung adenocarcinoma transcript 1 (lncRNA MALAT1) has gained significant attention due to its functional role in breast cancer, impacting various aspects of tumor biology and contributing to disease progression. This comprehensive study focused on the functional role of MALAT1 in breast cancer progression, exploring its impact on cellular processes and its potential as a diagnostic and prognostic marker.

Methods: Methods: This research was performed using articles published in various databases, including PubMed, Semantic Scholar, Science Direct,

Google Scholar and Cochrane between March 2014 and August 2023 then 45 references related to our keywords were reviewed.

Results: Results: It is exciting to study the functional role played by MALAT1 in breast cancer that reveals its multifaceted impact on various aspects of tumorigenesis and disease progression. The accumulated evidence underscores MALAT1 as a key player in breast cancer pathogenesis. Proliferation and Survival: Tripathi et al. showed that MALAT1 influences breast cancer cell proliferation by regulating the expression of cell cycle-related genes. Its upregulation results in increased cell division, driving tumor growth. Moreover, MALAT1's interaction with epigenetic modifiers contributes to cell survival, further promoting oncogenesis. Epithelial-to-Mesenchymal Transition (EMT): Earlier, Banyard et al. investigated that EMT is a critical process in cancer metastasis, and MALAT1's role in inducing EMT is well-established. By modulating EMT-related genes, MALAT1 facilitates the transformation of epithelial breast cancer cells into more invasive, mesenchymal-like phenotypes, ultimately enhancing the metastatic potential of tumors. Metastasis Promotion: Beyond EMT, MALAT1 enhances the migratory and invasive capabilities of breast cancer cells, facilitating their spread to distant sites. This metastatic promotion is a hallmark of advanced breast cancer and is associated with poor patient outcomes. Chemoresistance: Wu et al. underscore MALAT1's contribution to chemoresistance in breast cancer. Its upregulation is associated with decreased sensitivity to commonly used chemotherapeutic agents, presenting a significant clinical challenge. Competing Endogenous RNA (ceRNA) Activity: According to Yang et al. MALAT1's ceRNA function, whereby it sponges microRNAs (miRNAs), results in the activation of oncogenes and the suppression of tumor suppressor genes. This intricate mechanism of gene regulation impacts various signaling pathways, ultimately driving tumor progression. Diagnostic and Prognostic Marker: Wang et al, studied MALAT1's upregulation in breast cancer tissues that has been proposed as a diagnostic and prognostic marker. Elevated MALAT1 levels are associated with more aggressive tumor characteristics and poorer clinical outcomes.

Conclusion: Conclusion: To recapitulate, understanding MALAT1's functions in breast cancer not only deepens our knowledge of the molecular mechanisms underlying the disease but also presents therapeutic opportunities. Targeting MALAT1 through RNA-based strategies or small molecules may disrupt its oncogenic activities and improve treatment outcomes for breast cancer patients. Furthermore, this review emphasizes the importance of continued research in this area to unravel additional intricacies

of MALAT1's functions and to translate these findings into clinical applications, ultimately benefiting those affected by breast cancer.

Keywords: Keywords: Breast cancer, MALAT1, LncRNA

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Functionality of immune cells in COVID-19 infection: development of cell-based therapeutics (Review)

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Introduction: In late December 2019, a sudden severe respiratory illness of unknown origin was reported in China. In early January 2020, the cause of COVID-19 infection was announced a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Examination of the SARS-CoV-2 genome sequence revealed a close resemblance to the previously reported SARS-CoV and coronavirus Middle East respiratory syndrome (MERS-CoV). However, initial testing of drugs used against SARS-CoV and MERS-CoV has been ineffective in controlling SARS-CoV-2. One of the key strategies to fight the virus is to look at how the immune system works against the virus, which has led to a better understanding of the disease and the development of new therapies and vaccine designs.

Methods: This review discussed the innate and acquired immune system responses and how immune cells function against the virus to shed light on the human body's defense strategies.

Results: Although immune responses have been revealed critical to eradicating infections caused by coronaviruses, dysregulated immune responses can lead to immune pathologies thoroughly investigated. Also, the benefit of mesenchymal stem cells, NK cells, Treg cells, specific T cells, and platelet lysates have been submitted as promising solutions to prevent the effects of infection in patients with COVID-19.

Conclusion: In conclusion, the host immune responses are the crucial factor in destining COVID-19. Moreover, further analysis of these responses has indicated their effectiveness on the severity of the disease in different individuals, as some infected cases show mild symptoms, and others show no symptoms. Therefore, clear comprehension of these reactions in individuals with severe symptoms and carriers can better recognize the involved molecular mechanisms. Accordingly, with the help of which, not only can we pave the way to reach a long-term protective immunity against this virus, but also it might be possible to take preventive and therapeutic measures to overcome the outbreak of this virus and other kinds of CoVs. Cell therapy is a novel therapeutic method that prescribes cellular material for medical purposes. Different kinds of cells, including hematopoietic stem cells, mesenchymal stem cells, lymphocytes, NK cells, and DCs, can be utilized in cell therapy. At present, applying these cells to prevent or cure infected individuals of COVID-19 is undergoing clinical trials to gain full knowledge of their efficiency. It is hoped that this new medicinal approach can successfully treat patients diagnosed with COVID-19.

Keywords: COVID-19 SARS-CoV-2 Immune responses Cell therapy Innate Immune system Adaptive immune system

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Future of Osteogenesis with a Cannabis-made 3D Scaffold Coated with Reduced Graphene Oxide (Research Paper)

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Introduction: Nanomaterials (NMs) can improve scaffold behavior during tissue engineering. However, NMs have to be biocompatible and conductive, in addition to having particular mechanical and thermal properties, to be considered suitable for bone differentiation. These features of NMs allow surface improvements to establish an extracellular matrix suitable for better cell attachment, regeneration and proliferation of tissues. Reduced graphene oxide (RGO) has shown to bear the mentioned characteristics to promote osteogenic differentiation of stem cells to enhance bone formation. The purpose of this study was to use RGO as an NM to help improve the tissue engineering scaffold for human cell culture with specific aim of studying the differentiation of stem cells into osteoblast. We extensively investigated the suitability of RGO for use in cell culture. This included the attachment to scaffold and evaluation of surface morphology of RGO coated scaffold, chemical composition, hydrophilicity, biodegradability as well as its ability to support cell viability, proliferation, adhesion, and osteogenic differentiation. The high viability and proliferation of cells showed the biocompatibility of RGO. In addition, the expression of osteogenic differentiation of stem cell, showed its potential use in tissue engineering. Overall, these results suggest that RGO has favorable physiochemistry properties, which make it a suitable NM for cell culture. Future studies could investigate the performance of RGO in vivo and its potential use in regenerative medicine.

Methods: a

Results: a

Conclusion: a

Keywords: nanomaterial, osteogenic differentiation, tissue engineering

Gene network modeling and analysis in identifying genes causing resistance to paclitaxel in ovarian cancer (Review)

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Introduction: Introduction: Resistance to chemotherapeutic agents is one of the most important factors in the failure of cancer treatment. Ovarian cancer, one of the most common female cancers, is also affected by this problem. Treatment of this cancer is usually with the drug cisplatin, whereupon resistance to chemotherapy occurs. In this study, the molecular mechanisms and genes involved in the development of resistance to cisplatin during treatment of ovarian cancer will be investigated by gene network analysis and bioinformatics analysis.

Methods: Material and methods: In the present study, we analyzed a microarray dataset GSE50831 from the Gene Expression Omnibus (GEO) database and used Transcriptome Analysis Console v4.0 software to search OC cells for differentially expressed genes (DEGs). For functional annotation of DEGs, we used Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) using the STRING database. Protein–protein interaction networks (PPI) were also created using the STRING database, and Cytoscape software was used for visualization.

Results: Results: A total of 261 DEGs were identified in six samples from the GEO microarray dataset, of which 199 genes were upregulated and 62 genes were downregulated. GO Analysis of the subnetworks showed that the

biological process of DEGs mainly focuses on the regulation of DNA endoreduplication. Among the major molecular functions is the binding of the DNA replication origin. Cellular components include the BRCA1-B complex. KEGG pathway analysis of the subnetwork mainly focused on the p53 pathway, Fanconi anemia pathway and homologous recombination. In addition, 10 genes BRCA1, EXO1, CDC45, MCM10, CDKN1A, TOP2A, BRCA2, FBXO5, WDHD1 and FANCI were identified as hub genes. KEGG pathway analysis of the hub genes revealed that they are mainly involved in Fanconi anemia signaling, homologous recombination, and platinum drug resistance.

Conclusion: Conclusion: The results of this study demonstrate the importance of using bioinformatics analysis in identifying the molecular mechanisms of paclitaxel resistance in ovarian cancer. The genes and pathway obtained from this analysis likely play a role in paclitaxel resistance and can be considered as potential biomarkers for detecting paclitaxel resistance in ovarian cancer. However, further studies and experiments are needed to confirm the role of these genes and their signaling pathways in the development of drug resistance to paclitaxel in ovarian cancer.

Keywords: Keyword: Ovarian cancer, Paclitaxel resistance, A2780, Gene-network.

Generation of information diversity and DNA mutation based on the Quantum mechanics rules (Review)

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Introduction: In this theory, which is based on the quantum tunneling of the proton (hydrogen atom) of the organic base, the energy to move the proton can sometimes be supplied by ultraviolet waves irradiated to the body, but even so, it has not reached the amount of kinetic energy allowed to overcome the potential barrier, because the proton must first free itself from the potential resulting from the covalent bond. Here the concept of quantum tunneling can help. During the experiments, the proton of the organic base was replaced by deuterium, and because the mass of deuterium is greater than the mass of a proton, its tunneling probability is less, as a result, the mutation occurred at a lower rate. In such a case, a proton moves between A and T, or a proton moves between C and G. In the connection between organic bases in DNA, a hydrogen bond is established, and this hydrogen bond can be considered individually as a symmetrical potential well, according to the Schrödinger equation, the wave function in such a potential well has an oscillating response and has an even or odd parity and the probability of the presence of the particle on the left and right sides are equal to each other. According to the laws of quantum mechanics, two situations can occur when we reflect the wave function in the origin, which this wave function is the answer to the Schrödinger equation in a symmetric potential well. If the value of the wave function after reflection is the same as the wave function before reflection has even parity. If the value of the wave function after reflection is the additive inverse of the wave function before reflection it has odd parity. However, the probability of the presence of the particle, which is the square of the wave function, is the same on both sides. However, due to the presence of two hydrogen bonds near each other and disrupting each other's potential, the shape of the potential becomes slightly different, in other words, the proton potential of one organic base affects the proton potential of another organic base. Solving the Schrödinger equation for such a potential form is difficult, but at least it is clear that the particle can tunnel from left to right or vice versa. In the first case, the protons of both the upper and lower bands move in the opposite direction simultaneously. In such a case, the shape of the potential before and after the movement of the proton does not change, but the

potential of the upper and lower bond are reversed. Of course, it is also worth mentioning that normally, this proton transfer alone does not cause mutation, but after cell division and DNA replication, the mutation occurs because the shape of the organic bases has changed. In the second case, only one of the protons of the organic bases tunnels. After tunneling, the potential changes, and both organic bases become charged. This charge exists due to the interchange of hydrogen, which can be justified by examining the Lewis rule for the structure of the compound.

Methods: A review of articles on quantum biology and proton tunneling in DNA

Results: Most people consider the cause of DNA mutation to be external factors. Considering the effect of quantum mechanics on DNA mutation, it can be concluded that mutation also occurs by chance.

Conclusion: As quantum phenomena can occur at elementary particles, atomic, and molecular scales, it is essential to investigate their effects in biology and genetics.

Keywords: Quantum; Proton tunneling in DNA; Quantum biology

Genetic evolution Ophiocordyceps unilateralis (Research Paper)

Siamak Amirtaheri afshar,[1,*]

1.

Introduction: The common name of Ophiocordyceps unilateralis(O.unilateralis) is "zombie-ant fungi" who discover this fungi in 1859 by Alfred Russsel Wallace,base on many reasch done in this fungi they infected hardly in different species even in one family.by natural they never can be effected in complex species like human and whale because many reason like temperature of each species is different by each other and the temperature of O.unilateralis for feeding and coloning is 15 centigrad for that case they unable to infected a complex species. However for some reason of Gene expression they could move a body without any control by host and this movement can be observe for who hadn't any connection for them hands or legs ,we can use this fungi to discover of genes which they are silencing and needs to expression one more time to recovery a neuron of that part of body for cure a person who paralysis. We try evolution O.unilateralis by filling one lack of O.unilateralis with Crispr-Cas9 method in bioinformatic field to improve this fungi for more complex species to figure out which gene in complex species is expression and how it would be worked.

Methods: Crispr-Cas9 method in bioinformatic field

Results: O.unilateralis has some weakness like lack of toxin to defined complex immune system or need strength heat resistance to able live in all hosts body, for heat resistance we use crRNA-Cas9 to knock-in trehalose gene and make a another wall from glass to protect wall-cell from high heat.

Conclusion: In this process, we intend to use the evolution of the zombie fungus on other species to find out how genes are expressed and how this process works in order to gain a better understanding of the expression of complex genes in complex species such as humans. May we succeed in finding genes that are no longer able to be expressed and express them again in order to improve the medical industry and achieve progress that will never exist again, and this mushroom will help us in understanding muscle and nerve coding genes. It was that if we get a correct understanding of the expression of human nerve and muscle genes, we will be able to make the human organs move again.

Keywords: Crispr_Cas9 – bioinformatic – Gene expression – Genetic-fungal virulence – trehalose-carbon metaboli

Genetic Polymorphisms Associated with Susceptibility to COVID-19 (Review)

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Introduction: Introduction The COVID-19 pandemic, caused by the novel SARS-CoV-2 virus, has had a serious effect on global health and economies. One interesting observation is the profoundly variable clinical outcomes in individuals infected with the virus, ranging from asymptomatic cases to severe or fatal disease [1]. Clinical outcomes are impacted by several factors, including age, gender, and comorbidities. However, growing evidence recommends that host genetic factors play a significant role in modulating the susceptibility and severity of COVID-19[2]. This article reviews some of the key genetic polymorphisms that have been associated with susceptibility to COVID-19.

Methods: Genetic Polymorphisms and Disease Susceptibility Genetic polymorphisms allude to variation within the DNA sequence that are present in more than 1% of the population. These variations can influence an individual's susceptibility to diseases, including infectious diseases like COVID-19[3]. Several studies have been conducted to understand the relationship between genetic polymorphisms and COVID-19 susceptibility and severity. Here are some remarkable findings.

Results: ACE2 and TMPRSS2 Polymorphisms The ACE2 gene and the TMPRSS2 gene, which encode the angiotensin-converting enzyme 2 (ACE2) and the transmembrane protease serine 2 (TMPRSS2), respectively, play critical roles in SARS-CoV-2 entry into host cells [4]. Several studies have reported that polymorphisms in these genes may influence the susceptibility to COVID-19. A genome-wide association study (GWAS) conducted by Hou et al., recognized a few ACE2 polymorphisms related with altered ACE2 expression levels, potentially influencing the ability of SARS-CoV-2 to enter host cells [5]. So also, polymorphisms in the TMPRSS2 gene, particularly those impacting TMPRSS2 expression levels, have been associated with COVID-19 susceptibility [6]. HLA Polymorphisms The human leukocyte antigen (HLA) system is a vital part of the immune system, liable for presenting antigens to immune cells. HLA polymorphisms can impact the

immune response to infections, including SARS-CoV-2. A study by Nguyen et al. used computational methods to predict the binding of SARS-CoV-2 peptides to different HLA alleles and found considerable variation in binding abilities, suggesting that specific HLA alleles could potentially influence COVID-19 outcomes. [7] ABO Blood Group System The ABO blood group system has been associated with susceptibility to various diseases, including infectious diseases. Several studies have reported an association between the ABO blood group and COVID-19. A study by Zhao et al. found that blood group A was associated with a higher risk of COVID-19, while blood group O was associated with a lower risk. [8] Other Genetic Factors Several GWAS studies have identified other genetic loci associated with COVID-19 susceptibility and severity. A study by the Severe Covid-19 GWAS Group identified a gene cluster on chromosome 3 as a genetic susceptibility locus in patients with COVID-19 with respiratory failure [9]. Another GWAS by Pairo-Castineira et al. identified additional loci associated with COVID-19 severity, including genes involved in antiviral immunity and lung inflammation. [10]

Conclusion: Conclusion Whereas the identification of genetic polymorphisms related with COVID-19 susceptibility and severity provides profitable bits of knowledge, it's critical to note that these discoveries are preparatory and require further validation. In addition, genetic factors are just one piece of the puzzle, and other factors, such as age, gender, comorbidities, and environmental factors, also play remarkable roles in modulating COVID-19 outcomes. Nevertheless, understanding the genetic basis of COVID-19 susceptibility could potentially aid in the development of personalized risk evaluations and therapeutic procedures.

Keywords: polymorphisms , Genetic background ,SNP , COVID-19, infectious disease

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Genetics and its importance in Alzheimer's disease (Review)

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Introduction: Alzheimer's disease (AD) is a multifaceted and diverse neurodegenerative condition. There are currently 46.8 million dementia cases worldwide, and by the year 2050, there will likely be over 131.5 million cases. This study's objective was to look into genetics and how it relates to Alzheimer's disease.

Methods: Science Direct, Springer, Google Scholar, and PubMed were utilized as search engines in this investigation of genetics and its significance in Alzheimer's disease.

Results: Several novel genes that cause dementia illnesses have recently been discovered. Many insights have been crucial in helping us understand the aetiology of these illnesses. Most significantly, the discovery of disease-causing mutations in the genes for TAR DNA-binding protein-43 (TARDBP), progranulin (GRN), and C9orf72-SMCR8 complex component has furthered our understanding of frontotemporal dementia (C9ORF72). Additionally, the identification of uncommon variations in the gene for the triggering receptor expressed on myeloid cells 2 (TREM2) has brought attention to the role of inflammatory and immunological pathways in the development of AD. The analysis comprised nine genes with known pathogenic mutations causing familial early-onset dementia disorders (APP, PSEN1, PSEN2, MAPT, GRN, TARDBP, CHMP2B, VCP and FUS)

Conclusion: As a result, AD is a complicated neurological condition with a significant hereditary component. AD is a significant public health issue, and there is presently no cure or medication to stop AD from progressing. With the development of molecular genetics, numerous researches are being conducted in an effort to identify the genes causing both sporadic and autosomal dominant types of AD. Linkage analyses identified the AD genes APP, PSEN1, PSEN2, and APOE. GWASs have been discovered.20 loci linked to an increased risk of AD. The majority of the AD-related genes primarily fall into one of three groups: endocytosis, inflammatory response, and lipid metabolism. The identification of rare disease variations including PLD3, TREM2, UNC5C, AKAP9, and ADAM10 has been made possible by sequencing technologies.

Keywords: Alzheimer, PSEN1, CHMP2B, pathogenic

Genetics Factors in Major Depression Disease (Review)

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Introduction: One of the most prevalent types of psychiatric disease is depression (DD). The World Health Organization estimates that a DD affects roughly 350 million individuals. In most nations, the prevalence of DDs is between 8 and 12%, ranging from 3% in Japan to 16.9% in the USA. According to predictions, DDs will overtake ischemic heart disease as the second-leading global cause of disability by the year 2020. The serotonin transporter SLC6A4 (formerly known as SERT), which is responsible for the absorption of serotonin (5-HTT) from the synaptic cleft to the presynaptic neuron and hence plays a role in maintaining the serotonin level in the presynaptic area, has been the focus of the majority of investigations. Interest in this transporter also arises from the observation that inhibitors of neural serotonin reuptake are used widely in psychiatry for the treatment of depression, anxiety, and other conditions. The aim of this study was to investigate genetic factors in Major Depression Disease.

Methods: this review has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The structure of SLC6A4 may be far more complicated. Recent publications have reported that the expression of this gene is modulated by microRNA mir-16 binding sites in the 3′-nontranslated region of the gene. Therefore, polymorphisms localized within or near microRNA binding sites may be able to exert a strong effect on SLC6A4 expression and, consequently, on 5-HTT functions. It is possible that the abovementioned complexity of SLC5A4 organization may be one reason for the conflicting results obtained by analyses of the association of this gene's polymorphic variants (primarily in the analysis of the L/S polymorphism of the 5-HTTLPR repeat) with the onset of depression. Meta-analyses of these studies allow no final conclusion to be drawn about the role of this polymorphism in the development of depression. For instance, the meta-analysis conducted by Lopez-Leon et al. disclosed an elevated risk of DDs in S allele carriers, whereas no similar association was found in carriers of other alleles. The latest meta-analysis of the results of 23 original studies has shown that the S allele raises the risk of DDs; the risk of depression in S allele carriers is increased 1.14-fold (CI: 1.05–1.24). Nevertheless, the high level of heterogeneity of the data included in this meta-analysis should be noted. In all

analyzed models, the association p-value does not reach 0.05. This may be due to the inclusion in the meta-analysis of studies of different size samples, including samples comprising fewer than 50 people. In the context of the monoamine theory of DD development, analysis of a large number of candidate genes has been performed. They are, in particular, receptor genes for dopamine (DRD3, DRD4) and serotonin (HTR1A, HTR2A, HTR1B, HTR2C); genes for noradrenalin (SLC6A2) and dopamine (SLC6A3); genes for the enzymes monoamine oxidase A (MAOA), tyrosine hydroxylase (TH), tryptophan hydroxylase 1 (TPH1), catechol-o-methyl transferase (COMT); and the piccolo presynaptic cytomatrix protein (PCLO). For each of these genes, polymorphic variants were identified that were associated with point mutations or tandem repeat polymorphisms. These polymorphisms were analyzed in samples from patients of different ethnicities with DD. As for SLC6A4, different studies have produced conflicting results, and it seems reasonable not to analyze the results of individual studies but to consider only the meta-analyses that have shown the existence of associations between definite variants of the genes and DD development. One of the first large-scale meta-analyses of the genetic case–control research on DDs was conducted in 2008 by Lopez-Leon and coauthors. The final analysis focused on 20 polymorphisms in 18 genes. The pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Among the genes of the monoaminergic system, statistically reliable associations were found for SLC6A4 and SLC6A3.

Conclusion: Despite the drawbacks of such models, a three-pronged strategy that combines gene-association studies with assessments of the epigenetic status of DD patients and examination of the alterations in animal models of depression will allow researchers to pinpoint the contributions of genetic, epigenetic, and environmental factors to various forms of DDs and to create strategies for lowering the risk of depression and for providing adequate treatment.

Keywords: Genetics, Depression Disease, Serotonin

Genital herpes review article (Review)

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Introduction: Introduction: The number of patients with GH has increased by 30% over the past 10 years. The main role in the etiology of HSV belongs to HSV type 2 (HSV-2), but the pathogens of this pathology can become both HSV type 1 (HSV–1) and a combination of both types of herpes simplex virus.HSV-1 is mainly transmitted by oral-to-oral contact, whereas HSV-2 is almost exclusively transmitted sexually, causing genital herpes.HSV-2 has a key role in fueling the HIV epidemic and, although rare, HSV-1 and HSV-2 are associated with devastating outcomes when ac- quired during pregnancy, both among women and neonates. Upon primary infection, HSV will start its lytic replication cycle in epithelial cells, causing cold sores (mostly HSV-1) or genital sores (HSV-2). Eventually, the virus will invade sensory neurons, traveling retrogradely to the soma and establishing latency, particularly in the trigeminal and sacral ganglia for HSV-1 and HSV-2, respectively. From here, the virus can occasionally reactivate and travel anterogradely to the primary infection site, causing recurrence of the sores or genital herpes and enabling transmission to the next host. However, on rare occasions, HSV will instead invade the central nervous system (CNS), either during primary infection or at reactivation, thereby giving rise to herpes simplex encephalitis (HSE), brainstem encephalitis, or aseptic meningitis Analysis of systemrevealedatic studies among patients with COVID-19 revealed incidence rates of HSV reactivation detected by PCR technique, which can range from 12% to 83%.also Various studies have shown a higher prevalence of HSV infection or reactivation among cancer patients . For instance, the reactivation of HSV-1 was significantly associated with chemo-induced oral mucositis; however, whether HSV plays a major causative role in oral mucositis remains inconclusive.

Methods: Methods: These drugs help to speed healing of ulcers in people who have just been infected or in those who are having repeat outbreaks,fortunately consistent use of fungin ointment in the treatment and prevention of relapses of recurrent genital herpes showed high effectiveness in relieving symptoms in most patients, longterm remission was achieved, good tolerability was noted, and there were no complications. Some people

who have herpes outbreaks take medicine every day to prevent future outbreaks or prevent spread to their sex partner. There are ways to lowerl the risk of being infected with genital herpes. People should use a latex condom every time they have sex. Sex (oral, vaginal, and anal) is not recommended if a person has blisters or ulcers. Several vaccines and drug trials are in progress against HSV. They provide a promising therapeutic potential in individual studies. However, no profound and specific therapy has been established until now that could tackle the problem of HSV infection worldwide.

Results: Result: While symptoms of genital herpes can be managed and transmission to sexual part- ners prevented with antiviral therapy, novel therapies with new mechanisms of action will improve our ability to care for patients. Given that genital herpes affects a substantial proportion of adults, ongoing research to advance the field is urgently needed. According to the studies carried out in the United States ,finland,germany,Saudi Arabia and Iran,with the increase of age the transmission of HSV is elevated to a great extent,the prevalence of HSV-1 antibodies in girls was lower than boys and also individuals with lower education was more susceptible to HSV infection.

Conclusion: Conclusion: The need is to establish more coordinated and integrated studies with the cooperation of scientists, doctors, and pharmacies to take drug testing one step ahead in clinical practice. This is important because the expected viral mutations present the threat of the development of another HSV mutant that could then become another complication for HSV treatment and prevention. Therefore, the most effective approach for future therapeutic development will be to develop modern drug-design approaches such as those based on plant products and nanotechnology, and to carry out more combined therapies for large-scale and broad-spectrum antiviral and immunostimulatory effects. so that HSV complications can be successfully addressed in the coming years.

Keywords: Herpes simplex virus Epi.Cells Virus Review article Cancer Ovary

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Green Synthesis of Copper nanoparticles Derived by Green Tea Extract and Determination of Antimicrobial Effects on Staphylococcus auroras and Escherichia coli (Research Paper)

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Introduction: In this study, the aqueous extract of green tea plant was used to produce copper nanoparticles and its antimicrobial activity was investigated. To identify the synthesized nanoparticles, different analyses, techniques and tools were used, including and electron microscope, T.E.M imaging was performed and the size of the nanoparticles was determined.

Methods: method that was used is the XRD and Zeta potential methods, which according to the given graphs, each graph has alternating peaks, which shows the certainty of the synthesis. The antimicrobial activity of copper nanoparticles synthesized using the micro dilution method was used for bacteria in Mueller Hinton culture medium, which was used according to the CLSI standard. In this method, eight wells started with a concentration of 250 micrograms per milliliter and progressed half by half until well eight.

Results: In the extraction process, first 19g of green tea leaves and its ingredients were prepared and milled then it was soaked in 190 ml of distilled water, stirred well and placed in the refrigerator for 48 hours. Afterb48 hours 4 milliliters of the extract were added to one-tenth molar copper oxide to a volume of 25 milliliters, and it was placed on a heater shaker at a temperature of 80 degrees Celsius for one hour, after adding the extract to the colored copper oxide solution changed from black to light brown. Synthesized nanoparticles showed activity against Staphylococcus auroras and Escherichia coli bacteria.

Conclusion: The results showed that the aqueous extract of green tea plants acts as a rejuvenating and stabilizing agent. Synthesized copper nanoparticles showed activity against both gram-positive (Staphylococcus auroras) and gram-negative (Escherichia coli) bacteria.

Keywords: antimicrobial, copper, green tea, nanoparticles.

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Green synthesis of silver nanoparticles coated with Methotrexate-conjugated Polyvinyl Alcohol along with X-ray exposure on MDA-MB-231 breast cancer cell line (Research Paper)

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Introduction: Breast cancer is the most frequent cancer diagnosed in women worldwide. The main treatments include surgery, radiation therapy, and chemotherapy, but these treatments have many limitations and side effects. Methotrexate (MTX) is used in the treatment of many neoplasms. In the present study, we aimed to green synthesis of silver nanoparticles coated with methotrexate-conjugated polyvinyl alcohol and investigate the effects of combinational therapy following X-irradiation on tumor cells.

Methods: Size and surface charge, physico-chemical characteristics, and morphology of synthesized nanoparticles were investigated by DLS, FT-IR, UV-Vis, and FESEM. To assess blood biocompatibility, a hemolysis test was used. Various assays such as cell uptake, cell viability, and apoptosis were tested to investigate the increased radiosensitivity and anticancer effects of the synthesized nanostructures in both conditions with and without X-ray exposure.

Results: The physicochemical properties of synthesized nanostructures showed that the synthesis of nanostructures was successfully carried out. The results obtained from the cell uptake assay show the effective uptake of nanostructures by MDA-MB-231 cells. The Ag@PVA-MTX nanoparticles significantly reduced cell growth and increased apoptosis in both conditions with and without X-ray exposure.

Conclusion: Coating silver nanoparticles with polyvinyl alcohol and conjugating with methotrexate (Ag@PVA-MTX NPs) leads to an increase in radiosensitivity and as a result their therapeutic efficiency.

Keywords: Silver nanoparticles, Chemotherapy, Radiation sensitizer, Triple-negative breast cancer cell

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Gut Microbiota's Role in Calcium Balance: Implications for Health (Review)

Helia Hajiheidari,[1,*]

1.

Introduction: Microorganisms residing both on the surfaces and within the human body exert a profound influence on various physiological processes. Among these microbial ecosystems, the gut microbiome stands as the largest and most pivotal. Calcium disorders represent a significant health concern across numerous diseases, with conditions like chronic renal insufficiency leading to secondary hyperparathyroidism, a consequence of disrupted calcium homeostasis. Furthermore, disturbances in calcium regulation have been linked to aberrations in liver lipid metabolism via the calmodulator pathway, potentially culminating in conditions such as cirrhosis. Presently, a burgeoning body of evidence underscores the role of probiotics in augmenting calcium absorption.

Methods: reviewal

Results: This article provides a comprehensive overview of the intricate relationship between gut microbiota and calcium balance, encompassing key facets such as the impact of short-chain fatty acids, estrogen, immune factors, and vitamin D on calcium equilibrium. Additionally, it delves into the interface between gut microbiota, calcitonin, and bone metabolism, shedding light on the immunomodulatory effects of gut microbiota in the context of calcium balance. Furthermore, it explores the interplay between gut microbiota, vitamin D, and calcium absorption, as well as their influence on liver function and serum calcium levels.

Conclusion: Microorganisms residing both on the surfaces and within the human body exert a profound influence on various physiological processes. Among these microbial ecosystems, the gut microbiome stands as the largest and most pivotal. Calcium disorders represent a significant health concern across numerous diseases, with conditions like chronic renal insufficiency leading to secondary hyperparathyroidism, a consequence of disrupted calcium homeostasis. Furthermore, disturbances in calcium regulation have been linked to aberrations in liver lipid metabolism via the calmodulator pathway, potentially culminating in conditions such as cirrhosis. Presently, a burgeoning body of evidence underscores the role of probiotics in augmenting calcium absorption.

Keywords: Gut Microbiota, Calcium Balance, calcium absorption

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hAMSCs secretome enables to regulate Smad2/3/4 expression in HT-29 colon cancer cells (Research Paper)

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Introduction: One of the main causes of mortality worldwide is colon cancer. It was shown that the current cancer therapy platforms are not effective and thereby, exploring new strategies with high effectiveness remains a major challenge. Due to unique biological characteristics of stem cells, it is considered that stem cells is a potent promising platform in cancer therapy. The aim of this study is evaluation of human amniotic mesenchymal stromal cells (hAMSCs) secretome effects on Smad2/3/4 expressions in HT-29 colon cancer cell.

Methods: We are interested to evaluate the effects of hAMSCs secretome on Smad2/3/4 expressions in HT-29 colon cancer cells. To do so, we employed a co-culture system using Transwell 6-well plates. After 72h, hAMSCs-treated HT-29 cells, Smad2/3/4 expressions were analyzed using western blot method.

Results: The significant down regulation of Smad2/3/4 expressions in HT-29 cells after 72h treatment with hAMSCs by using western blot was demonstrated.

Conclusion: Our results support the idea that hAMSCs may be a unique and effective therapeutic approach to treat colon cancer cells.

Keywords: HT-29 colon cancer cells, hAMSCs, Smad2/3/4 expression

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Helicobacter pylori and its Gastric cancer related factors. (Review)

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Introduction: Cancer is a complex disease that usually deevlops over time through multiple steps. Inflammation caused by bacteria is a significant contributor to the development of cancer. The inflammation can increase cell division, leading to cancer growth.Not all bacterial strains are carcinogenic, but some can be. For instance, H. pylori has been known to cause GC.Over 90% of patients with GC have either a current or previous H. pylori infection.

Methods: Several virulence-related genes have been identified in the Helicobacter pylori genome, including cagA, vacA, iceA, babA, dupA, hpaA. The development of GC is associated with H. pylori virulence factors.

Results: Nearly all cases of GC are caused by H. pylori infection. Eradicating H. pylori can prevent GC progression. Quadruple therapy (bismuth quadruple and concomitant) is the recommended first-line treatment. However, antibiotic resistance is becoming more prevalent and is often the reason for treatment failure.

Conclusion: The causes of gastric cancer are varied and involve environmental, genetic, and epigenetic factors as well as host-related issues. While H. pylori infection is necessary, it alone is not enough to cause gastric cancer. Lifestyle changes and dietary habits can also help to reduce the incidence of GC. It is important to identify high-risk patients and offer personalized therapy by targeting precursor lesions as part of prevention strategies.

Keywords: H. pylori, Gastric cancer, Related virulence factor to GC.

hematological research during pregnancy (Review)

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Introduction: Pregnancy is associated with various physiological changes that continue immediately after conception until delivery. During this period, physiological changes and various hematological manifestations occur in women. During pregnancy, the pregnant mother undergoes significant anatomical and physiological changes. Pregnancy and breastfeeding are physiological periods that lead to an increase in metabolic needs. During pregnancy, an increase in plasma volume and red blood cell mass, as well as an increase in plasma protein synthesis, occur. Also, during this period, a physiological hemodilution occurs, which leads to a decrease in the plasma level of some vitamins, if the plasma level of some vitamins cannot change due to carrier enhancers. Vitamin B12 is essential for maintaining body health and folate metabolism for cell proliferation during this period.

Methods: Vitamin B12 is essential for maintaining body health and folate metabolism for cell proliferation during this period. Vitamin B12 is associated with an increased risk of pregnancy and complications and adverse outcomes such as preeclampsia, spontaneous abortion, intrauterine growth spurt, preterm birth, megaloblastic anemia of the newborn, malformation of the fallopian tube, and neurological problems in the newborn. The main observed blood changes include physiological anemia, leukocyte and immunological function, mild thrombocytopenia and coagulation and fibrinolysis. Anemia is the most common blood abnormality in pregnant women, which can lead to maternal and fetal complications. The main cause of anemia in pregnancy is iron deficiency, which increases the need for iron. Physiologically, the most common cause of anemia in pregnancy is iron deficiency anemia, which occurs in order to increase the need for iron during this period.

Results: Pregnancy can be associated with numerous hematological manifestations. Rapid diagnosis and early treatment are often necessary to prevent maternal and fetal complications.

Conclusion: The number of lymphocytes decreased in the first and second trimester of pregnancy and increased in the third trimester, which is lower compared to non-pregnant women, and then returns to its normal value 4

weeks after delivery. The number of monocytes is higher in pregnancy, especially in the first trimester, but it also decreases as the pregnancy progresses The ratio of monocyte to lymphocyte increased significantly during pregnancy, while the number of eosinophils and basophils did not change significantly during pregnancy. In healthy women with normal pregnancy, there is no change in the absolute number of lymphocytes, as well as the relative number of B and T lymphocytes.

Keywords: Pregnancy, anemia in pregnany, hematologic manifestations, bleeding in pregnancy

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Herbal Medicine and Covid19 as a new research (Review)

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Introduction: At the end of 2019, the coronavirus outbreak due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) happened in Wuhan, Hubei, China, leading to the quick spread of2019 novel coronavirus (COVID-19) into a pandemic responsible for the ongoing global health crisis. Coronavirus can be treated by proper nutrition. An evidence showed that vitamin D diminished the risk of COVID-19 outbreak. Many herbs and foods are known to show antiviral and immunomodulatory activities. Aloe vera, Angelica gigas and Astragalus membranaceus have been reported to immunomodulatory features. In this review, we decided accumulation some data in patients and we want to gain better way for treatment of COVID

Methods: narrative review

Results: Propolis used in prevention or treatment of COVID-19(500 mg/day), 3 to 4 times per day Also, it could be applied in more severe cases of COVID-19, with higher dosages. Caffeic acid phenethyl ester (CAPE), one of the most important constituents of propolis, stopping or preventing covid19-induced fibrosis in the lungs. propolis, the vegetal source is of extremely crucial from Europe and Asia, generally made by bees from resins collected from Poplar trees has flavonoid compounds. In latest years, there have been a number of reports on the herbal compounds as adjuvant for enhancing efficiency of minor immunogenic vaccines.(5) Propolis has effects that are relevant to SARS-CoV-2 infection. Propolis has historically been hugely used to alleviate dissimilar diseases. propolis has a vast spectrum of pharmacological behavior and is a dietary supplement which is commonly consumed by healthy and sick people. It is also used in veterinary medicine, due its antifungal, antibacterial, antiviral, and immunomodulatory activities.(3) The herb Glycyrrhizae radix et rhizome, can be used for every stage of diseases. we found that the Glycyrrhizae radix et rhizome just appears in one herb pair. Studies show that compounds such as glabridin, gallic acid and quercetin present in Glycyrrhizae radix et rhizoma may handle angiotensin-converting enzyme 2 (ACE2) for the treatment of COVID19. Glycyrrhizae radix et rhizoma seem to play main role in every stage of COVID19

Conclusion: Herbal medicine could be applied as supplement to prevent infection and supportive therapy in combination with validated anti-COVID medications to modulate the humoral and cellular immune responses, to restrict co-infections or reduce virus titers. Europe has a long tradition of using medicinal plants for many diseases for therapeutic purposes. In this way, a bridge between science and tradition, would have a strong effect on the capacity for treatment and prevention of COVID-19

Keywords: immune system; COVID-19; complementary and alternative medicine; coronavirus disease; herbal medicin

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Hesperidin suppressed Tumor Growth and increased cell survival on Induced Breast Cancer in BALB/c Mice (Research Paper)

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Introduction: Introduction: Hesperidin, a flavonoid, have been shown various biological effects including anticancer activity. The objective of the study was to investigate the protective effects of hesperidin against experimentally induced breast cancer in BALB/c.

Methods: Methods: In this study, we treated 4T1 tumor-bearing Balb/c mice with intraperitoneal injection of Hesperidin, Hesperidin +Doxorubicin, and saline as control groups. Body weight and tumor volume were measured before and after treatment. Hematoxylin and eosin (H & E) staining and immunohistochemistry of Ki-67, MMP2, MMP9, VEGF and E-cadherin markers were used as markers of proliferation. The effect of hesperidin on changes in tumor growth and survival rate was also investigated

Results: Results: The average tumor volume, average pCR and the percentage of destroyed tumor cells were lower in the hesperidin group with different doses than the normal saline group ($P \geq 0.05$) and the percen survival was significantly higher ($P \geq 0.05$). Also, the expression of Ki-67, VEGF, MMP2, MMP9, E-cadherin markers in the hesperidin group with different doses was significantly lower than the normal saline group. The expression of these markers in the hesperidin + doxorubicin group (10+20 mg) was lower than the normal saline group and the doxorubicin 10 mg group ($P \geq 0.05$).

Conclusion: Conclusion: The results of this study confirm that hesperidin can be considered as a potential suitable treatment both in the presence of standard treatment (doxorubicin) and without it. The role of hesperidin as an inhibitor of tumor growth and increased cell survival was observed in this study. Therefore, it is suggested to design and conduct corresponding clinical studies to confirm the effect of hesperidin on breast cancer in humans.

Keywords: Keywords: Angiogenesis, Phatology, Breast cancer, Hesperidin

High yield Expression and Purification of A. flavus Uricase Cloned in Pichia pinkTM Expression System (Research Paper)

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Introduction: Enzyme-based drugs are part of a very diverse group of protein drugs that catalyze reactions specifically and with minimal interference with biochemical processes (1, 2). Rasburicase, the recombinant form of uricase, is one of the most well-known enzymes in the treatment of various origins of hyperuricemia in humans, which are caused by its evolutionary deletion in the metabolic pathways of uric acid decomposition or complications caused by chemotherapy such as tumor lysis syndrome (3, 4, 5). Its homotetrameric structure in Aspergillus flavus has 301 amino acids in each subunit with a molecular weight of 135 kDa (6). This enzyme was recognized as a suitable substitute for allopurinol in the treatment of hyperuricemia, which has a clear relationship between this condition and tumor lysis syndrome, blood pressure, coronary heart disease, and progressive kidney failure, because the resulting allantoin has ten times more solubility than uric acid. It does not have the harmful effects caused by the accumulation of xanthine and hypoxanthine due to the use of allopurinol (7,8). With the existence of injectable vials for the treatment of hyperuricemia, efforts have been started to test the oral drug enzyme, especially in the cause of renal failures (9). Various prokaryotic and eukaryotic hosts have been used to express rasburicase. One of the first transformations of Aspergillus flavus uricase gene and comparing its expression with the mutant of the same gene was done by Chevalet et al. (10). Initial attempts to clone Aspergillus flavus uricase were made by Legous et al. in E. coli (11). Since then, uricase gene from different sources such as rat, Nilaparvata lugens insect, Arthrobacter globiformis, Bacillus subtilis,

Candida utilis, Pseudomonas aeruginosa and Kluyveromyces marxianus has been cloned as a gene construct in different hosts such as E. coli, Saccharomyces cerevisiae and Pichia pastoris (12-19). Among the reasons for the production and use of the recombinant form of uricase (rasburicase) instead of its non-recombinant form under the brand name Uricozyme, is the lower heterogeneity of rasburicase, as well as the 50% increase in specific activity and the removal of host protein and nucleic acid impurities in its production process pointed out (20). Therefore, high-scale expression and maintaining catalytic activity have been among the challenges of producing therapeutic enzymes, which depends on the type of gene expression vector, the host, and the purification strategy used (19). The engineered pichia pink strain not only has the advantages of its mother strain, Pichia pastoris, including protein processing, proper folding, post-translational modifications, and more than a tenfold increase in the expression of heterologous proteins compared to S. cerevisiae, but also due to the gene complementation process (Complementation) ADE2 causes easy selection of colonies expressing the target gene, compared to the antibiotic resistance method, and on the other hand, due to the knockout of cellular proteases, it reduces their effects and removes the need for heavy protease inhibitors (21, 22). In this research, the synthetic DNA sequence of uricase enzyme was expressed intracellulary after codon optimization using the Ppink-Uox expression vector in the Pichia Pink strain, and after optimizing the expression methods in the fermentor scale, cell lysis and purification, the enzyme was produced with medicinal and industrial potential.

Methods: The DNA sequence of urate oxidase (UOX) enzyme was synthesized as PUC57-UOX after codon optimization of Pichia pastoris by GeneScript, USA, and it was used for the transformation of susceptible E. coli Top10 cells. The selected vector for Pichia Pink strain was pPink-HC product of Invitrogen. In order to connect UOX gene to pPink-HC, both vectors were enzymatically digested by EcoR1 and Kpn1 enzymes on 1% agarose gel. Isolation of the UOX gene and the linearized plasmid pPink-HC was performed on agarose gel using the recovery kit of Vivantis company with catalog number 70028C. After making the pPink-UOX expression vector, BTX model ECM630 device with 1800 v, 200 A and 25 ohm parameters was used for electroporation. The enzyme used to linearize the final construct was spe1. After screening the colonies expressing uricase in YPD solid medium, colony PCR was used to confirm the presence of its gene in the recombinant yeast. Using a single colony of transformants, 10 ml of YPD culture medium was inoculated and shaken for 24 hours at 30 degrees at 250 rpm and it was used to inoculate 200 ml of liquid YPD medium until reaching OD600=2-3. The cells were centrifuged at 1500 g for 5 minutes and after discarding the supernatant, the pellete was dissolved in YPD containing 25% glycerol so that the final

OD600 reached 100-50 (approximately 5.2-5.1 x 109 cells per milliliter). The cells were aliquot into new vials, frozen by liquid nitrogen and kept at -80°C. Expression of recombinant uricase A single recombinant clone containing UOX gene was inoculated in 10 ml of BMGY medium, then shaken at 30°C and 150 rpm. After centrifugation of the grown cells using Falcon at 1500 g for 5 minutes, the supernatant was discarded and the remaining pellete was dissolved in 10 ml of BMMY medium. After 17±1 hours, 100 microliters of 40% methanol was added to each of the falcons that had been shaken at 150 RPM and at a temperature of 28 ˚C, and they were shaken again with the same conditions as before. After other 17±1 hours, samples were prepared for enzyme activity measurement. After selecting the two colonies with the highest enzyme activity, the cells were induced to express UOX in the presence of different percentages of 0.5, 1 and 3% methanol in BMMY culture medium for 96 hours. To start the fermentation process, after defreezing the cell bank at 37 °C, 400 microliters of it was added to 400 ml of BMGY culture medium and harvested after 17±1 hours incubation and harvested when reaching OD600=3±1 to inoculate the fermantor media. Semi-defined culture medium (SDM) was selected as the fermenter media and the first and second feeds were determined as 400 ml of glycerol (50% w/v) and 1400 ml of methanol (100%). Fermentation was done in a 5-liter Labfors5 model fermenter. The pH of the SDM before inoculation was adjusted to 5.2±0.2 and maintained at this point by adding ammonium hydroxide. After 19±1 hours of inoculation with spike of oxygen, which indicates the complete consumption of glycerol and the beginning of the fedbatch step, glycerol (50% w/v) was added to the culture medium as the first feed at a rate of 20 g/L/h. After the completion of the glycerol feed and the second oxygen spike, 100% methanol as the second feed was started at a rate of 7ml/L/h and reached 26ml/L/h after 48 hours. Finally, after 60 hours and using 1700ml of 100% methanol, it was harvested. 15ml samples were taken every 6 hours to check cell dry weight, OD600, enzyme activity and SDS-PAGE test. Optimal protein expression was performed using 12% SDS-PAGE by adding 25 µl of samples to each well. Bradford's test was also used to determine the protein content. downstream processes Cell lysis Regarding the intracellular expression of recombinant uricase, the following steps were taken to release the enzyme in an active form for every 200 mg of biomass: 200g of harvested biomass in 2L lysis buffer (50mM sodium phosphate, pH=7.4, 1mM PMSF as a protease inhibitor, 1mM EDTA, 5% glycerol) was dissolved at 4°C. The resulting solution was homogenized using a homogenizer (GEA Lab Homogenizer Panda PLUS 2000) in 4 passes at a pressure of 900 bar and treated with PDADMAC 0.05% for 1 hour before centrifugation for 20 minutes at 9000 rpm. Purification of recombinant uricase Ultrafiltration/Diafiltration (UF/DF) In this step, using the lysis buffer and the tangential flow filtration device (TFF 300 kDa) made by Pall Corporation, USA, during 7 cycles, most of the impurities

with a molecular weight greater than 300 kDa are removed and the target enzyme is permeated by the 30 kDa filter using the equilibrium buffer (7mM NaH2Po4, 3mM Na2Hpo4, pH=6.5, conductivity=6.5±0.1mS/cm) was concentrated during 7 cycles. Before applying the UF/DF retentate to the column, it was filtered using a 0.22 µm Millipak filter. FPLC To purify tag-free recombinant urate oxidase (uricase) protein, three consecutive columns in GE ÄKTA FPLC™ were used as follows; In the first step of chromatography, the target protein was removed from the DEAE XK Sepharose column in flow through mode. This column (4 x 16 cm, GE Healthcare) was equilibrated using the equilibration buffer used in the TFF device, and in order to maintain the temperature of 4 °C, cold water was circulated through the column and after loading the harvested sample with a resident time of 5 min from the resin was passed. This step was done to remove the host proteins and bind them to the resin, and the recombinant uricase removed from the resin was taken on the CM sepharose column to obtain greater purity. In this column, in addition to the previous equilibrium buffer with pH=6.5 and conductivity=1.35±0.1 mS/cm, Elution buffer with the same formula but with pH=7.86 and conductivity=1.35±0.1 mS/cm and also 2M NaCl as H.salt was used. Finally, the CM column fractions was placed on the Phenyl Sepharose XK 16/20 column with equilibrium buffer (7mM NaH2Po4, 3mM Na2Hpo4, (NH4)2SO4 pH=7.38±1, conductivity=151±1mS/cm), wash buffer (7mM NaH2Po4, 3mM Na2Hpo4, (NH4)2SO4 pH=7.38±1, conductivity=109±1mS/cm), and Elution buffer (7mM NaH2Po4, 3mM Na2Hpo4(NH4)2SO4 pH=7.38±1, conductivity=68±1mS/cm) for final purification. Enzyme specificity analysis, reverse phase chromatography (RPC) and size exclusion chromatography (SEC) were also performed based on the method described in (26). Enzyme activity assay Cell lysis was performed in the expression step in the Erlen and Fermentor scale due to the small volume of the sample using the glass bead method (27). The investigation of uricase enzyme activity was done in all steps after the harvest of the fermenter using UV spectrophotometry optimization (28). 1 ml of the supernatant obtained from the cell lysis step was centrifuged at 14000 rpm for 20 minutes at 4 ˚C. To prepare the standard curve as a positive control, 10 microliters of standard enzyme was added to 290 microliters of boric acid buffer (1 Iu/ml). 20 microliters of the resulting solution was added to 580 microliters of uric acid solution and 13 readings were made using spectrophotometry at a wavelength of 293 nm with 10 second intervals. Enzyme activity was calculated using the following formula: units/ml Enzyme=((ΔA293/min⁡〖test-ΔA293/min⁡〖blank〗〗 〗 (0.6)(DF))/((12.3)(0.02)) 0.6= whole reaction volume per minute 12.3= uric acid extinction coefficient 0.02= volume of enzyme per milliliter

Results: Determination of target gene and recombinant expression vectors PUC57-UOX and pPink-UOX. Analysis of uricase, PUC57-UOX and pPink-UOX gene constructs by SDS-PAGE shows that the target gene sequence is correctly placed in the target vectors and between the cutting site of KpnI and Ecor1 enzymes. The uricase gene was under the control of the alcohol oxidase promoter to make the pPink-UOX expression plasmid. To confirm the construction of the recombinant vectors, they were digested with the aforementioned restriction enzymes (Figure 1). Figure (1): Analysis of the stages of cloning, screening and small-scale expression of the recombinant uricase gene. (A) Molecular weight marker (1), undigested vector pPink-HC (2). Linear pPink-HC vector (3), undigested pUC57-UOX (4), pUC57 vector (upper 5) and uricase gene (lower 5), which were both separated by KpnI and Ecor1. (B) Confirmation of uricase gene cloning in pPink-HC after enzymatic digestion and extraction of pPink-HC vector fragments and the target gene (lines 1 and 3 above and below). (C) Linearization of pPink-UOX gene construct with Spe1 enzyme (1), molecular weight marker (2) and non-linear construct pPink-UOX as control (3). (D): Colony PCR results and confirmation of the presence of recombinant uricase gene in the vector of several colonies of 9 Pichia Pink yeast colonies (2 to 9) and molecular weight marker (1). (E) Small-scale expression of recombinant uricase(rUOX) and its SDS-PAGE results in different colonies at three different times 0 (before induction), 24 and 48 hours after cultivation in BMMY medium. Expression of recombinant uricase Finally, after examining the best uricase producing colonies on the Erlen scale, their expression level and enzyme activity were checked in the presence of different percentages of methanol, and one of the colonies was selected for production on the fermenter scale. As the results of SDS-PAGE in Figure (2A) show, the 2D clone on the Erlen scale and with the presence of 0.5% methanol after 96 hours had the higher expression and enzyme activity (0.7 IU/ml) compared to clone 2B and was used for the fermentation process. Both clones showed better performance in the presence of 0.5% methanol, so that the expression and enzyme activity decreased in the presence of 1% and 3% methanol (data not shown). Recombinant uricase comprises 12% of total cellular proteins. Figure (2) SDS-PAGE analysis of recombinant uricase expression in Erlen and Fermentor scales. (A): Expression of two selected colonies in the presence of different percentages of methanol induction after 96 hours. Colony number 2B in the presence of different percentages of methanol 3% (1), methanol 1% (2) and methanol 0.5% (3). Colony number 2D in the presence of different percentages of methanol 3% (4), methanol 1% (5) and methanol 0.5% (6). Urate oxidase standard (7), negative control (8) and molecular marker (9). (B): Recombinant urate oxidase expression in Pichia pink at different hours of Fedbatch fermentor. Molecular markers (1 and 10). 12 h- 60 h of Fermentor fedbatch (3-8 and 12- 14). Negative control (2 and 11). Standard urate oxidase (9 and 15). The conditions for inducing

expression in the fermentor-scale were optimized so that there is maximum expression of the enzyme intracellularly. The lysis of cell samples taken from different stages of the fermentor, with increasing hours, showed an increase in expression and also an increase in enzyme activity. The highest yield of intracellular production of recombinant uricase was obtained in semi-defined medium with pH=5.2±0.2, 28±0.5 ˚C, 30% dissolved oxygen, aeration speed 430 rpm, and pressure 0.3±0.1 bar during 60 hours fermentation. About 19±1 hours after inoculation and spike of oxygen in glycerol feed (50% w/v) for 6 hours and following the oxygen spike, 100% methanol was added to the culture medium. Continuous induction with methanol was continued for another 54 hours until its harvest. A separate band of about 34 kDa related to the monomers of recombinant uricase appeared after 18 hours of induction using methanol, which was not visible in the previous hours and became more colorful as the induction hours increased (Figure 2B). Chart (1): Changes of OD600 in different hours of the fedbatch of the fermenter run Fermentor inoculum had OD600=0.273, and at the end of the batch step, this value reached OD600=72 and the cell dry weight reached 30 g/L. Finally, after 60 hours, the OD600 reached 490 and the cell dry weight reached 103 g/L. (Charts 1 and 2). Chart (2): changes in cell dry weight at different hours of the fedbatch of the fermenter run The maximum biomass produced in a fermenter with a culture medium volume of 4 liters is 1500 grams. Considering that glycerol was the first feed of the fedbatch step and this feeding continued for 6 hours and then 100% methanol feeding was started as an inducer of recombinant uricase expression. Therefore, until 12 o'clock in this step, no enzyme activity is observed during sampling. Chart (3): Enzyme activity changes (IU/ml) at different hours of the fedbatch of the fermenter With increasing amount of biomass, with the passage of time, the expression of recombinant uricase also increased, which was accompanied by an increase in enzyme activity (Figure 2B and Figure 3). The enzymatic activity of recombinant urate oxidase reached 2.44 U/ml 6 hours after induction with methanol, and after 60 hours of fermentation it was 14.54 U/ml, which was obtained by glass bead lysis, which showed both expression and very good activity of the enzyme. Purification of recombinant uricase Using a 5-liter fermenter, 1500 grams of biomass was obtained from 4 liters of semi-definite culture medium. All purification steps were performed at 4 ˚C. The target enzyme was purified using three consecutive columns: DEAE sepharose (flow through mode), CM sepharose (capture mode) and Phenyl sepharose (capture mode) after cell lysis and preparation of supernatant (explained in materials and methods). As the SDS-PAGE results of each step show, at the end, a high purity of 99% of the recombinant uricase is obtained. Figure (3) SDS-PAGE analysis of purification steps of recombinant uricase. (A): first step of purification using DEAE sepharose column. Molecular weight marker (1). uricase standard (2). before TFF 300 kDa (3). Permeate 300 kDa (4).

Retentate 300 kDa (5). Permeate 30 kDa (6). Retentate 30 kDa (7). Initial (8). Flow through (9). H. salt (10). (B): The second purification step using CM sepharose column. Initial (1). Molecular weight marker (2). Flow through (3). Eluate1(4). Eluate2(5). Eluate 2-1(6). Eluate 2-2(7). Eluate3(8). uricase standard (9). (C): third purification step using Phenyl Sepharose column. Molecular weight marker (1). Initial (2). Wash (3). Eluate (4). H. Salt (5). uricase standard (6). The use of 300 kDa and 30 kDa TFFs, respectively, caused the removal of most of the impurities. The DEAE Sepharose column was run in flow through mode and the recombinant uricase was passed through the column without binding to the resin (Figure 3A). By taking the peak of this step on the CM Sepharose column in capture mode, another major part of impurities is removed (Figure 3B) and eluate peaks with the target enzyme of this column, finally using Phenyl Sepharose resin with a purity of more than 99% of urate oxidase was purified (Figure 3C and Figure 4). The summary of information related to each purification step is given in Table (1). The final yield of recombinant uricase per liter of culture medium was 120 mg. The analysis of the results of RP and SE chromatography shows the purity, hydrophobicity, degraded form and aggregated form of standard enzyme (Figure 5). Figure (4): Chromatogram of the third step of purification using Phenyl Sepharose column The final product was kept for 4 weeks to test the stability of the activity at 4 ˚C (data not shown). Table (1): Purification of recombinant uricase Purification step Volume (ml) Total activity (U) Total protein (mg) Specific activity(IU/mg) Yield Purification (fold) P.pink cell lysate 1000 2500 6596 0.37 100 1 DEAE Sepharose 500 1750 1827 1 70 3 CM Sepharose 308 1190 338 4.37 68 13 Phenyl Sepharose 104 750 31.25 24 63 65 For long-term storage of the enzyme, it was stored through a sterile 0.22 µm filter at -80 ˚C using 20 mM phosphate buffer with 1% mannitol and 1.6% alanine. Figure (5): Size Exclusion Chromatography and Reverse Phase Chromatography analysis results of recombinant uricase. (A): SEC analysis of standard sample. (B): SEC analysis of recombinant uricase. (C): RPC analysis of standard sample. (D): RPC analysis of recombinant uricase.

Conclusion: The results of the present research show the successful use of pichia pink yeast in cytosolic expression of recombinant uricase. Creating a new approach in the purification steps of this enzyme led to a purity of over 99%, which is comparable to the biochemical characteristics of the standard enzyme. Choosing Pikia pink as a eukaryotic host and changing the purification approach that can be used in the industry were two unique features in this study, which together enabled the production of recombinant uricase with high expression and optimal preservation of enzyme activity. According to our knowledge up to now, the present study has comprehensively improved the defects in the industrial production of previous studies in terms of host selection, higher expression and the purification

approach that can be used in the industry to obtain optimal high enzyme activity.

Keywords: Uricase, Pichia pink, FPLC, Rasburicase

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How Artificial intelligence is Transforming Cancer Care (Review)

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Introduction: Nowadays numerous anticancer curatives are available but choosing a cure for cancer continues to be a delicate task. Still, with the arrival of artificial intelligence (AI), there's a new stopgap for advanced cancer care. AI has the implicit to revise the way we diagnose and treat cancer. It can dissect vast quantities of patient data, identify patterns and trends, and develop individualized treatment plans as well as accelerate medicine discovery and development. AI-powered imaging is helping doctors to identify cancerous cells more directly and snappily, while machine algorithms are being used to prognosticate patient issues and present treatment opinions. AI has the implicit to revise cancer care by perfecting patient issues, reducing costs, and accelerating exploration and development. Still, ethical considerations must be taken into account to ensure that the benefits of AI are balanced against patient safety. This paper will explore the part of AI in cancer care.

Methods: We investigated Scopus and PubMed databases from 2018 through 2022 with a keyword combination of “cancer/AI applications” and “cancer artificial intelligence”. Based on the aim of the search, outcomes of interest included studies investigating the role of AL in diagnosing, treating, and preventing cancer.

Results: In cancer, AI can be applied to different types of data, including medical images, genomic and proteomic data, exploring electronic health records (EHRs), and medicine discovery and development. One of the most promising areas of AI in cancer is medical imaging. AI offers an excellent progressive occasion to medical imaging technology. It is grounded on computational models and bioinformatics- algorithms that can determine any abnormal cellular growth and natural changes in the body. AI- image analysis

can be applied to different types of medical images, including CT, MRI, and positron emigration tomography (PET) to describe changes, shape, and texture that may not be visible. They can also be used to prognosticate treatment response and prognostic on changes in size and metabolic exertion. For illustration, algorithms have been used to describe lung nodes on CT with high delicacy and prognosticate response to chemotherapy. Another area of AI in cancer is genomics. Genomic data provides precious information about the molecular characteristics and can be used to prognosticate treatment response and prognostic. This analysis can be applied to genomic data, including gene expression, mutations, numbers of variations, and epigenetic variations that can be used to identify new remedial targets based on the molecular characteristics of cells. Several AI- genomic analysis tools have been developed for various types of cancer. For instance, algorithms have been used to prognosticate response to immunotherapy in carcinoma on the presence of specific mutations. AI- EHR analysis is another area that contains precious information about case demographics, medical history, and treatment issues that be used to prognosticate treatment response and prognostic. In this case, Machine algorithms have been used to prognosticate the threat of colorectal cancer on EHR data. AI is also making a significant impact in medicine discovery and development. Still, there are also ethical considerations that must be taken when using AI in cancer care. One of the main one is patient safety. AI algorithms must be designed to cover patient data and ensure that it isn't misused or participated without the case's satisfaction. In addition, there's a threat that AI algorithms may be make incorrect prognostications, which could have serious consequences for patients.

Conclusion: In conclusion, AI is an evolving field that holds great hope for cancer diagnosis, treatment, and monitoring. AI-tools have shown promising results in preclinical and clinical studies. The integration of multiple AI tools into the medical field is likely to give us the most accurate and individualized approach to cancer care.

Keywords: Cancer, AI, machine learning, Genomic data, cancer artificial intelligence

HPV cancer review article (Review)

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Introduction: Cancer ranks as the first or second leading cause of death before the age of 70 in more than half of the world's countries, according to a (WHO) report . It is estimated that infectious agents cause of all human cancers, with viruses accounting for 10–15% of all cases. The main viruses that cause cancer in humans include hepatitis B and C , human herpes (HHV-8), human T lymphotrophic type 1 (HTLV-1), Epstein–Barr (EBV), and human papillomavirus (HPV)

Methods: HPV is linked to nearly 5% of all cancers worldwide . associated with a variety of serious cancers, such as gastrointestinal (Colorectal,Anal,Gasteric,Esophageal,Liver cancer) , cervical, urinary bladder, and head, and neck cancers(Oral squamous cell carcinoma, Hypopharygeal and Laryngeal cancer).

Results: Over 100 HPV types have been described, papillomaviruses are classified into low-risk (LR) and high-risk (HR) HPV types. LR-HPV types, including types 1, 2, 6, and 11, are non-carcinogenic types and they do not induce cancerous lesions. They can benign lesions (warts, condylomas, or recurrent respiratory papillomatosis) or, in rare cases, precancerous lesions . HR types, including 16, 18, 31, 33, .., because they induce 99.7% of cervical cancers and other anogenital cancers. HPV infection concerns both women and men, but cervix an ideal tissue to complete the viral lifecycle it is transmitted through sexual contact by all contact points. Epidemiological and clinical data also inform about various non-sexual modes of transmission especially at the time of birth and by close contact. HPV is small and non-enveloped virus with double-stranded circular DNA . HPV genome is divided into three regions: 1. The non-coding region, which affects the replication and transcription 2. The early region, which encodes E1, E2, E4, E5, E6, and E7 proteins 3. The late region, which encodes L1 and L2 as capsid proteins. E6 and E7 proteins of the early region have an essential role in the oncogenic properties of HPV . they promote excessive cell cycle proliferation by interfering with regulatory proteins such as p53 and pRb. The virus entry to be achieved via binding to heparin sulfate proteoglycans in the epithelial basement membrane via L1. The virus capsid then undergoes a conformational change allowing the exposure of L2, This newly exposed site on L2 binds to surface molecules on the wound keratinocyte, and that there

the capsid undergoes a further conformational change and that the cellular receptor binding site on L1 is exposed. The virus binds via L1 to the cellular receptor, and cell entry is accomplished. Cervical cancer is the fourth most common female malignancy worldwide . Squamous cell carcinoma and adenocarcinoma account for nearly 70% and 25% of all cervix cancers caused by HPV infection, respectively. HPV 16 and 18 are associated with two-thirds of cervical cancer and subsets of cancers of the vulva, vaginal, penis, anus, oropharynx, and skin. Cervical cancer relieves further copies of the chromosome arm 3q, which contains the hTERC gene in the 3q26 location. This gene is considered to be a template for telomerase RNA, which are responsible for the repeat sequence, which enhances tandem to the ends of chromosomes to maintain the telomere length. As a result, abnormal hTERC amplification leads to increased proliferation, resulting in cervical tumors. expression of the hTERC has the potential to act as a biomarker for the diagnosis and prognosis of cervical neoplasia.

Conclusion: Detecting markers that existence of cancers help to improve the treatment and control of cancer before the final stages of the tumor. One of these factors is the p16 protein, one of the inhibitory proteins of cyclin-dependent kinases. Overexpression of this factor in HPV is due to the inhibitory effect of E7 on Rb. Another factor is the level of expression of P53, which may be mutated or inhibited. In many cancers, detecting antibodies against P53 can help in the early diagnosis of cancer. Currently, what is considered a cancer-tracking agent is HPV ctDNA. This factor is released into the blood due to the destruction of cancer cells, and they believe that identifying this marker can help initiate cancer treatment.

Keywords: HPV, cancer, viruse, E7, E6

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hpv virus (Review)

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Introduction: Papillomavirus genome is comprised of a small doublestranded and highly conserved DNA with an approximate size of 8000 base pairs and consists of three regions.that belonging to the Papovaviridae family. According to its genotypic nature, the HPV virus can lead to benign proliferative changes such as warts or cancers in different parts of the body. In the first case, the virus is considered a low-risk type and in the second case, it is considered a high-risk or cancerous type. About two hundred types of this type of virus are known, of which more than forty types are colonizing in the genital tract. For a more detailed explanation about the structure of the virus is that: There are six ealy proteins , three regulatory proteins (E1,E2, and E4) three oncoproteins (E5, E6, and E7)encoded in 4000 base pairs (bp) that participate in viral replication and transformation of cell . another 3000 bp region of dna molecule encodes two structural proteins L1 and L2 that compose the capsid of virus. the viral dna replication and transcriptional regulatory elements are controlled by long control region (LCR)that is encoded in a 1000 bp region .

Methods: the present literature review was performed using pubmed (national institute of health .ncbi.nlm.nih.gov/pubmed) , scopus (elsevier, scopus.com/scopus/home.url)and web of knowledge(thomson reuters,wok.mimas.ac.uk)electronic databases,and the following key words were searched : the role of human papiloma virus in cancer progression , viruse , human papilloma infection and cervical cancer . hpv molecular biology .several article were found in the surveyed databases and only the most relevant ones published in high impact factor journals and conducted by groups with recognized knowledge in the area were selected .

Results: HPVs can infect basal epithelial cells of the skin or inner lining of tissues and are categorized as cutaneous types or mucosal types. Cutaneous types of HPV are epidermitrophic and target the skin of the hands and feet. Mucosal types infect the lining of the mouth, throat, respiratory tract, or anogenital epithelium.most hpv infections are beneign and was first recognized as a cause of cutaneous warts such as planter , flat, common warts on the hands and feet . Benign types of the virus mainly include types6,11,42,43 and malignant types mainly include

16,18,31,33,34,35,39,45,51,52,56,58,59,66,68,70 those that lead to vulvar, anal, oral, penile, cervical, and oral cancers.

Conclusion: In most cases, the body removes this virus from the body without the person knowing, and the created warts also disappear. But in cases such as a weak immune system and high-risk types such as type 16and 18, smoking and long-term contact with this virus, this virus can cause cancer in the body. Prevention of high-risk behaviors and compliance with hygiene and periodic examinations in case of suspicious symptoms and use of condoms are ways to prevent contracting this virus.

Keywords: human papilloma virus, cancer, warts, benign , malignant

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HPV-associated oropharyngeal cancer (Review)

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1.

Introduction: HPV is the most common sexually transmitted disease worldwide. The risk of contracting it at least once in a lifetime among men and women is estimated at 50%. Although HPV infections are asymptomatic and resolve within 2 years, approximately 10% of people develop persistent infection, and their risk of developing head and neck cancer increases. The most common types of HPV are 16 and 18 in cancers of the genital tract and cancers of the mouth, throat, and digestive tract. Genotypes 6 and 11 cause more anogenital warts and respiratory papillomatosis but are rarely associated with cancer. The purpose of this review is to organize the evidence of the association between HPV infection and oral and pharyngeal cancers.

Methods: Oropharyngeal squamous cell carcinoma (OPSCC) Human papillomavirus HPV+ is one of the fastest growing cancers among young people. HPV 16 accounts for approximately 95% of oral and pharyngeal cancers with HPV+. HPV-related head and neck tumors have different characteristics from HPV HNSCC. Patients are younger and often non-smokers and do not consume alcohol. Meanwhile, alcohol and tobacco consumption are the most important factors for head and neck cancer. In addition, HPV-related OPC in Populations with higher social and economic class are seen. OPSCC is detected in the advanced stages of the disease due to the lack of early symptoms. Unlike tobacco- and alcohol-related squamous cell carcinomas of the head and neck (HNSCC), patients with HPV-related OPSCC have shown significantly higher cure rates.

Results: Identification of PMHC:HPV16/18 complexes with high avidity may be a way to expand antitumor therapies for different patient populations. Effective immunotherapy for HPV HNSCC requires a combination of therapeutic approaches to overcome adaptive immune resistance as the tumor continuously evolves with exposure to different therapies. Elucidating the details of the immune evasion mechanism of HPV is important to control its persistent infection. During the oncogenic process, the extrachromosomal HPV genome often integrates into the host genome. HPV genome integration is the most important factor associated with stable and high expression of E6 and E7 oncoproteins. However, many of these integrations may be silent integrations due to increased overall genetic instability.

Conclusion: Integration includes induction and high expression of E6 and E7 in the host, which leads to cell cycle activation and increased genomic stability. This integration leads to disruption of E2 expression. By binding to ubiquitin ligase, E6 protein breaks down P53 protein and by increasing cell telomerase activity, immortalizes cells and inhibits apoptosis. E7 protein activates E2F by binding to pRb (retinoplasma), which leads to cell cycle activation and increased genomic instability of the host. The different characteristics of HPV-related oropharyngeal cancer have led to clinical trials to test new treatment strategies. Today, simultaneous chemotherapy has established its role as a definitive adjuvant treatment option after surgery for patients with advanced regional disease. In untreatable recurrent or metastatic conditions, the emergence of immunotherapy and biological drugs, both alone and It has been added to our armamentarium in combination with chemotherapy to relieve patients' symptoms, optimize disease control and prolong survival.

Keywords: Cancer HPV oropharyngeal sexually transmitted disease Oropharyngeal squamous cell carcinoma

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HSV-1 Infection and Parkinson's Disease Risk: Mechanisms and Implications (Review)

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Introduction: Parkinson's disease (PD) is a neurological disorder and the second most common neurodegenerative disease in the over-65 population, whose prevalence will nearly double by 2030; it is characterized by symptoms such as resting tremors, muscle rigidity, bradykinesia, and postural instability. Additionally to host genetics and environmental factors, pathogens can play a role in Parkinson's disease (PD). Herpes simplex virus type 1 (HSV-1) is a DNA virus that can induce herpes and is a member of the herpesviridae family of pathogens. HSV-1 is widespread in the brain of persons in the latent form and can infect the central nervous system (CNS), which is connected with the severity of Parkinson's disease; As a side effect of HSV-1 viral encephalitis, signs of parkinsonism appear. Disruption of the body's immune system may play a part in Parkinson's disease autoimmunity by reactivity with the human amyloid protein alpha-synuclein (α-synuclein).

Methods: A systematic search was conducted from 2010 to 2023 in scientific databases such as PubMed, Scopus, Google Scholar, and the World Health Organization (WHO) website. The purpose of the research was to investigate the molecular biology, immunology, and genetics of HSV-1 infection in patients with Parkinson's disease and healthy controls. The search terms included "Parkinson's disease," and "HSV-1".

Results: The protein α-synuclein, which is compacted in the presynaptic terminals of dopaminergic neurons in the pars substantia nigra and has a crucial role in the start and progression of neurodegeneration in Parkinson's disease. Furthermore, the existence of molecular mimicry regions in α-synuclein that stimulate immunological cross-reaction with the HSV-1 peptide (UI42) can cause nerve injury, and the response with antibodies generated against HSV-1 in past infections can accelerate the progression of PD disease. On the other hand, HSV-1 infection can cause the accumulation and deposition of -synuclein in the brain by altering the microbiota composition of the intestinal nervous system and the production of curli protein from its producing bacteria, thereby accelerating the neurodegenerative process in PD

patients. HSV-1 can alter the host's innate immunity, particularly the immune response mediated by interferon-β (INF-β), by decreasing the stimulation of anti-inflammatory cytokines such as interleukin-10 (IL-10) and increasing serum inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-1 beta (IL-1β), causing impaired and diminished immune reactions in PD. Moreover, chronic exposure to IL-1β causes an increase in the expression and deposition of -synuclein, as well as increased injury in PD patients. However, HSV-1 infection induces inefficient production of the antiviral cytokine interferon-lambda (IFN-λ), resulting in HSV-1 reactivation and increased damage to PD patients. Also, the oxidative stress caused by mitochondrial dysfunction promotes viral replication in cells damaged by viral infection, which contributes to the development of Parkinson's disease in patients.

Conclusion: Since the exact cause of Parkinson's disease (PD) is unknown and the prevalence of HSV-1 infection in over 70% of the global population and its lifelong persistence in the olfactory bulb leads to an increasing effect on brain cells in PD, interactions between HSV-1 and host immune and genetic factors can modulate the clinical outcome and severity of PD. Therefore, a greater understanding of the complex relationship between the nature of HSV-1 and its specific immune responses in patients with PD can facilitate the development of effective antiviral therapies and vaccines to prevent the advent of PD.

Keywords: Parkinson's disease, herpes simplex virus type-1, α-synuclein, cytokines

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Human papilloma virus and cervical cancer review article (Review)

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Introduction: Cancer remains one of the leading causes of death during the last few decades. Despite the advancement of early diagnosis and treatments, a number of new cancer cases and cancer-related deaths are predicted to increase worldwide with the aging population. HPVs representing the most common sexually transmitted disease are a group of carcinogenic viruses with diffrent oncogenic potential. Vaginal microbiome represent the modifiable and important risk factor in HPV-induced carcinogenesis. HPV infection significantly increases vaginal microbiome diversity and induces local inflammation, leading to gradual increases in the abundance of anaerobic bacteria and consequently the severity of cervical dysplasia. Anaerobic bacteria produce pro-inflammatory mediators and induce oxidative stress with subsequent epigenetic alterations resulting in formation of tumor microenvironment. Delineation of the exact composition of the vaginal microbiome, epigenetic state of cervical epithelium and immune environment before HPV acquisition, during persistent/progressive infections and after clearance, provides insights into the complex mechanisms of cervical carcinogenesis. It gives hints regarding the prediction of malignant potential.

Methods: Relative high HPV prevalence in the general population is a challenge for modern and personalized diagnostics and therapeutic guidelines. Identifying the dominant microbial as well as epigenetic and immune response biomarkers of high-grade and low-grade dysplasia could help us to triage the patients with marked chances of lesion regression or progression. Any unnecessary surgical treatment of cervical dysplasia could negatively affect obstetrical outcomes and sexual life. Therefore, understanding the effect and role of microbiome-based therapies is a breaking point in the conservative management of HPV-associated precancerous lesions. Sequentially, the immune response and epigenetic rearrangement of cervical epithelium could help to control the therapy outcome. Qualitative and quantitative assessment of local microbial environment and associated risk factors constitutes the critical background for preventive, predictive, and personalized medicine that is essential for improving state-of-the-art medical care in patients with cervical precancerous lesions and cervical cancer.

Results: Although the microbiota has largely been associated with the pathogenesis of viral infections, most studies using omics techniques are correlational and hypothesis-generating. The mechanisms affecting the immune responses to viral infections are still being fully understood. Here we focus on the two most important sexually transmitted persistent viruses, HPV and HIV.

Conclusion: Human microbiome study has become pivotal during the last years; eubiosis, pathobiosis, and balanced ecosystem are now leading terms in comprehension of Health and Disease in humans.Increasing interest in human microbiome has recently been focused on “eubiosis”: symbiotic balance between human cells, lactobacilli and other species of bacteria, fungi or virus

Keywords: Hpv Human papilloma virus papilloma virus probiotics

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Huntington's disease, symptoms, diagnosis and treatment (Review)

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Introduction: Huntington's disease was first described by American doctor George Huntington in 1872, while his grandfather also noticed this disorder, that's why this disease is known as Huntington's. This disease is the most common monogenic neurodegenerative disease in the Western world, which is a brain disorder that is caused by mutations in the Huntingtin gene and is transmitted in an autosomal dominant manner. and as a result of multiple repetitions of cytosine, adenine and guanine (CAG) in the coding region of the gene located in the short arm of chromosome 4. Before the discovery of the HD gene, it was pointed out that the age of onset of HD is related to the gender of the affected parents, but with the discovery of that gene, it was found that the earlier the age of onset, the higher the number of triple repeats for a given patient. In people with this disease, the number of CAG repeats, the age of onset of the disease, and the severity of the symptoms are different. For the normal HTT gene, which is a wild type gene, there can be between 6 and 26 of these repetitions, and more than 26 repetitions lead to problems. People who have 27 to 35 repetitions are unlikely. get HD, but they can transmit this disease to the next generation. People with 36 repetitions or more of HD and more than 40 repetitions have full penetrance of the disease. This disease also has a juvenile form that is expressed with more than 60 repetitions.

Methods: All the information obtained about Huntington's genetic disease was done through searching terms such as disease diagnosis method, symptoms, treatment, prevalence and mortality statistics in Google Scholar's reliable scientific database from 12019 to 2023, and in the end, a general summary of 21 valid scientific review and research articles was made. And a series of important and significant information was collected and included in this article.

Results: According to the research conducted, the prevalence of the disease worldwide is widely different between men and women, and Western populations such as Canada, the United States, England, and Australia have the highest prevalence. While African and Asian countries such as Japan, Korea, Thailand and Hong Kong have a lower prevalence of the disease; In general, this disease is estimated between 4 and 10 cases per 100,000. The

disease may begin at any age and may be asymptomatic for years. Its occurrence is usually in the middle-aged period of the late 3rd or early 4th decade, but 6% may occur under the age of 20. The symptoms of HD are in three areas: motor, cognitive and psychiatric, where behavioral disorders and symptoms usually precede motor characteristics, and depression is the most common. . Other symptoms are endocrine disorders, homeostasis changes, immune changes that increase cytokines, and psychiatric symptoms are involuntary choreic movements. In the movement symptoms, it is abnormal in two ways, involuntary or voluntary, which causes problems in walking. HD disease can be diagnosed through clinical symptoms and genetic testing, but it is difficult to determine when a person has changed from an asymptomatic carrier to a diseased state.

Conclusion: Current treatments are mostly limited to treating symptoms because there are no treatments to prevent the onset or slow the progression. Tetrabenazine is the only drug approved for the treatment of the disease in North America and some European countries, however, it can increase depression as a potential side effect. In Europe, antipsychotic drugs are often used. In the last decade, there has been a great growth in potential therapeutic targets and clinical trials, and due to the monogenic nature of the disease, they are seeking to inhibit the expression of the HTT gene, so that they can directly target the primary disease mechanism.

Keywords: Huntington's disease / gene / HTT / HD

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Hyper accumulation of C-phycocyanin by Arthrospira platensis in succinate-fed pulse cultivation mode (Research Paper)

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Introduction: The A. platensis is a multicellular, filiform, helical-shaped, and photosynthetic blue-green prokaryotic microalgae. It is greater than most species and is simply/quickly ingested and absorbed in the human body owing to the lack of cellulose in its cell wall. The A. platensis is one of the most fascinating microalgae, which can be applied for the manufacturing of functional foods, cosmetics, antioxidant colorants, neutaceiticals, supplements, medicine, due to their relatively high contents of vitamins, minerals with many health profits (counting antitumor, reductant inhibitor, antiviral, antiphlogistic effects, etc.) as well as positive influences against mal-nutrition, fatness, diabetes, anemia, etc. without any undesirable secondary effect on human fitness. A. platensis is a protein-rich cyanobacterium (60–70% (w/w)) and a promising source for c-phycocyanin (47% of the total proteins). It has double colorants including phycobiliproteins; allophycocyanin (APC) and c-phycocyanin (CPC), which originates 15–20% of dry cell mass. Consistent with Future Market Insights, c-phycocyanin worldwide market worth will each a value surpassing $232.9 million, by the end of 2025. Moreover, it has been reported that biomass production of A. platensis in the open pond was usually lower than 0.8 g L−1 and contained only around 7% phycocyanin content. Several studies have tried to improve A. platensis biomass and phycocyanin yield with cultivation governing, such as pre-harvesting, nitrate-fed cultivation. Glutamate and succinyl–Coenzyme A are amongst the transitional metabolites in the biosynthesis of tetrapyrroles such as phycobilin and chlorophyll, in algal and cyanobacteria cells. In other words, the sodium glutamate and succinic acid are substrates that could activate the phycocyanin increase as consequence of metabolic pressure.

Methods: The Arthrospira (Spirulina) platensis were fed batch cultured in Zarrouk medium. The initial nitrate concentration was 2500 mg L−1, the first pulse day was 8th day of cultivation period, and the addition concentration of sodium glutamate and succinic acid was 5 mmol L−1/ 7.5 mmol L−1, and the second pulse day was 12th day of cultivation period, for both treatments.

Results: The maximal Allophycocyanin and Phycocyanin production was obtained for pulse day succinic acid addition at 19th day of cultivation ($p<0.05$). The high Allophycocyanin concentrations (0.2 And 0.31 mg mL−1) were obtained for sodium glutamate and succinic acid pulse day addition, respectively, while phycocyanin concentrations reached to 0.14 and 0.23 mg mL−1.

Conclusion: Succinic acid is a C4-dicarboxylic acid produced as a key intermediate of the tricarboxylic acid (TCA) and tetrapyrroles biosynthesis. As a widely investigated high-value chemical, it has numerous applications in the fields of agriculture/aquaculture, green solvents and pharmaceuticals. Several studies indicated that TCA cycle intermediates were able to function as chemical stimulators for motivating zeaxanthin accumulation in Flavobacterium multivorum. Besides, exogenous Succinic acid improved stimulated Larix olgensis cultivating growth by effective photosynthesis and antioxidative properties. In the present study, the high Allophycocyanin/phycocyanin concentrations ((0.2 And 0.31 mg mL−1) / (0.14 and 0.23) were obtained at 19th day of cultivation, for pulse fed succinic acid and sodium glutamate, respectively. In contrast, in another study Allophycocyanin accumulation of 0.116 and 0.114 mg mL−1 was obtained for sodium glutamate and succinic acid cultivation, respectively. Once more, applying sodium glutamate / Succinic acid combined with nitrate feeding strategy, they obtained phycocyanin concentrations of 0.212 and 0.234 mg mL−1. Based on our results succinate pulsed cultures exhibited higher Allophycocyanin and Phycocyanin accumulation compared to Glutamate pulse culture. These data evidenced the choice of the succinic acid as intermediate precursor source for the cultivation of A. platensis. Therefore, addition of substrates in the fed batch (pulse day) regime has boosted phycocyanin content, then again succinic acid was found to be the best substrate for Allophycocyanin hyperaccumulation as well as high phycocyanin production.

Keywords: Arthrospira platensis, metabolic stress, Succinic acid, phycocyanin, overproduction

Hypothesis of Cancer Hygiene: Helminths play a significant role (Review)

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Introduction: Chemotherapy and surgery are traditional cancer treatment options, but they often come with severe side effects and limitations. In addition to killing cancer cells, chemotherapy can also harm healthy cells. Advanced-stage cancers may not be amenable to surgery, although it works for localized tumors. On the other hand, immunotherapy has been bringing new hope to treating cancer. The hygiene hypothesis states that children living in ultra-hygienic environments, especially those free of viruses, bacteria, parasites, and helminths, are more likely to develop cancer. Several pathogenic microorganisms have been used in cancer immunotherapy for many years. An objective of this review is to examine previous literature that has been published on tumors and helminths.

Methods: The search was conducted in several databases, such as Scopus, PubMed, Google Scholar, and Web of Science, for articles published between January 2000 and January 2023 that examined the antitumor effects of helminths. 700 studies have been funded as a result of keyword searches on topics such as Hygiene, Helminths, Parasites, Cancer, and Cancer immunotherapy. According to the abstracts, 500 studies were excluded, and 200 were given full-reading texts to examine. During the study, 50 articles relevant to this topic were selected with complete abstracts to be included in the analysis.

Results: There is mounting evidence that helminths induce immune modulation in tumor microenvironments, suppressing tumor-promoting inflammation, enhancing antitumor immune responses, and restoring normal

immune balance. Based on preclinical studies, Echinococcus granulosus, Trichinella spiralis, Toxocara canis, and Taenia solium may reduce tumor growth, induce apoptosis, and modulate the tumor microenvironment. Cancer patients can benefit from helminth therapy if the treatment reduces tumor growth, stimulates the immune system, and improves survival rates. However, there is limited research to support these claims. A combination therapy, such as antigen selection and immune profiling, as well as an individualized approach based on helminth therapy, may be an avenue for improving treatment outcomes. It is possible for helminths to produce bioactive molecules directly targeting cancer cells or that their microenvironment influences the production of such molecules. There are several molecules with anticancer properties, including glycoproteins, proteins, and excretory secretions. Specific helminth-derived proteins are capable of causing apoptosis, inhibiting angiogenesis, and inhibiting metastasis in cancer cells. The antitumor properties of helminths are attributed to their stimulation of immune cells. In addition to enhancing the activity of natural killer cells (NK cells), which can recognize and destroy cancer cells directly, they may also promote the production of cytokines. Helminths may also trigger the production of cytokines that suppress excessive immune responses and attract regulatory T cells (Tregs). Helminths control chronic inflammation and inhibit tumor growth in addition to regulating the immune system.

Conclusion: The use of helminth-based therapy for cancer treatment is becoming increasingly popular, especially with the use of Trichinella spiralis, Echinococcus granulosus, Toxocara canis, and Taenia solium. It has been demonstrated that those helminth antigens can modulate the immune response as well as directly cause cytotoxicity in cancerous cells. In addition to offering better outcomes, helminth therapy offers fewer side effects and personalization. It would be possible to revolutionize cancer therapy through the combination of helminth properties with existing treatment modalities and provide a new avenue for healing for those suffering from cancer everywhere. Helminth therapy may improve treatment outcomes when combined with traditional cancer treatments. A more comprehensive and efficient cancer treatment plan can be developed with helminth therapy and chemotherapy, radiotherapy, or immunotherapy combined.

Keywords: Hygiene Helminths Parasites Cancer Cancer immunotherapy

Identification of diagnostic biomarkers via Weighted Correlation Network Analysis in colorectal cancer using a system biology approach (Research Paper)

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Introduction: Colorectal cancer (CRC) is the third most frequent cancer to be diagnosed in both females and males necessitating identification of effective biomarkers. An in-silico system biology approach called weighted gene co-expression network analysis (WGCNA) can be used to examine gene expression in a complicated network of regulatory genes.

Methods: In the current study, the co-expression network of DEGs connected to CRC and their target genes was built using the WGCNA algorithm. GO and KEGG pathway analysis were carried out to learn more about the biological role of the DEmRNAs.

Results: These findings revealed that the genes were mostly enriched in the biological processes that were involved in the regulation of hormone levels, extracellular matrix organization, and extracellular structure organization. The intersection of genes between hub genes and DEmRNAs showed that DKC1, PA2G4, LYAR and NOLC1 were the clinically final hub genes of CRC.

Conclusion: To sum up, the bioinformatics strategy used in the current study revealed important roles of DKC1, PA2G4, NOLC1, LYAR, and E2F1 in the CRC carcinogenesis and potentiates these genes as biomarkers for detection of CRC and therapeutic targets for this cancer.

Keywords: Colorectal cancer, WGCNA, Transcriptome analysis

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Identification of hub Genes and pathways in hepatitis B virus-associated hepatocellular carcinoma (Research Paper)

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Introduction: The hepatitis B virus is one of the most common causes of liver cancer in the world. This study will assist us in providing effective treatment by gaining a better understanding of the mechanisms involved in the development and progression of HBV-related cancer. By identifying hub genes and the pathways related to their functions, we can improve the diagnostics and treatment of diseases.

Methods: An analysis of GSE83148 from the Gene Expression Omnibus (GEO) site was carried out as part of this study. In this study, we were able to identify DEGs with a p-value < 0.02 and a log |FC| >1.9 by normalizing the data using R software. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) databases were used to identify pathways involved in the process of hepatocellular carcinoma development. We performed an analysis of protein-protein interactions (PPIs) by using the software Cytoscap and Gephi to identify the hub genes based on the results of the PPI analyses. A GEPIA analysis was carried out to be able to confirm the biomarkers and the target genes used in this study.

Results: A total of 418 DEGs have been identified. Through the use of PPI, 96 hub genes were identified. According to the results of the GEPIA analysis, 3 genes with higher levels of expression in tumor samples have been identified as biomarkers, such as PPP2R1A ($p < 0.05$), TPR ($p < 0.05$) and TYMS ($p < 0.05$). It has been found that these biomarkers are involved in pathways related to Positive Regulation Of Protein Import Into Nucleus, Protein-Containing Complex Organization, one carbon metabolism and AMPK . There was a possibility of increasing survival rates by targeting genes like MTHFR ($p = 0.0026$) and RHEB ($p = 0.016$). by targeting these genes and reducing their expression, it was possible to increase survival rates, There are a number of pathways involved in target genes, including Autophagosome

Membrane Docking ,Methionine Metabolic Process, Cellular senescence, and Endocytosis.

Conclusion: We concluded that the integrated bioinformatics approach was effective in revealing the pathways involved in the development process of HCC. By identifying hub genes. It will be possible to detect this disease at the earliest stages of the disease, and with the identification of target genes, it has been possible to increase survival rates.

Keywords: Hepatocellular carcinoma, HBV, PPI network, Diagnostic biomarkers, Cancer targeted therapy

Identification of key genes in Amyotrophic lateral sclerosis through systems biology (Research Paper)

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Introduction: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by progressive destruction of motor neurons. To date, there is no treatment to stop or slow the progression of the disease, and the diagnosis is mostly based on clinical symptoms. Identification of ALS biomarkers can be important for early diagnosis, especially in the early stages, as it can improve patients' quality of life and prolong survival. Therefore, this study aimed to discover the hub genes and important pathways associated with ALS.

Methods: A gene expression profile of Amyotrophic lateral sclerosis (GSE4595) was obtained from the gene expression omnibus (GEO) available at https://www.ncbi.nlm.nih.gov/geo. GSE4595 included 9 healthy controls and 11 ALS samples, which analyzed by R programming language to screen differentially expressed genes (DEGs) between ALS and normal samples. Genes with p-value < 0.05 and |logFC| ≥ 1.0 were considered as DEGs. Enrichment analysis of ALS-related genes was conducted by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway using Enrichr available at https://maayanlab.cloud/Enrichr. The protein-protein interaction (PPI) network of identified DEGs was reconstructed using the Search Tool for the Retrieval of Interacting Genes (STRING) database (http://string-db.org/) and visualized by Cytoscape 3.9.0 software. CytoHubba plug-in and degree centrality were employed to identify 10 hub genes. Moreover, MCODE was used to identify top structural modules in the PPI network.

Results: A total of 676 DEGs were found after integrated analysis between ALS and normal samples. Among them, 501 were up-regulated and 175 were down-regulated. GO biological process demonstrated that DEGs are associated with chemical synaptic transmission, gluconeogenesis, signal release from synapse, neurotransmitter secretion, regulation of cation channel activity, cellular response to copper ion, and regulation of NMDA receptor activity. GO Molecular function indicated that DEGs are related to tubulin binding, calcium ion binding, metal ion binding, proton transmembrane transporter activity, phospholipase inhibitor activity, ATPase binding, oxidoreduction-driven active transmembrane transporter activity, and

syntaxin-1 binding. GO cellular components showed a relationship between identified DEGs and neuron projection, axon, vesicle, dendrite, extracellular membrane-bounded organelle, proton-transporting V-type ATPase, V1 domain, and clathrin-coated vesicle membrane. Furthermore, KEGG pathway enrichment analysis showed an association between DEGs and Pathways of neurodegeneration, Alzheimer disease, Parkinson disease, Prion disease, Synaptic vesicle cycle, Huntington disease, Phagosome, and cGMP-PKG signaling pathway. In PPI network reconstruction, a total of 437 nodes and 1924 edges were existed. Based on degree, 10 genes including SNAP25, CYCS, SLC32A1, SNCA, GABRG2, SYT4, GABRA1, GAD2, GAP43, and ATP5A1 were selected as hub genes.

Conclusion: In this study, the crucial genes and pathways in ALS progression were identified. Based on top three modules related to ALS, SNAP25, CYCS, SLC32A1, SNCA, GABRG2, SYT4, GAD2, and ATP5A1 genes may have potential values for diagnosis and prognosis of ALS. Further experimental validation studies are needed to confirm these findings.

Keywords: Amyotrophic lateral sclerosis, ALS, Network-based analysis, Systems biology, Biomarker

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Identification of Potential and Novel Biomarkers Based on Drug Resistance in Two Different Type of Glioma Cell Lines. (Research Paper)

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Introduction: Glioma is a common tumor originating in the brain. About one-third of all brain tumors are gliomas. Temozolomide resistance is an essential challenge in the management of patients with glioma. This study aimed to introduce hub genes that play a role in the treatment resistance of glioma, and further, reveal two different prognostiv models based on two different glioma cell lines.

Methods: Gene expression data of resistance and sensitive glioma cell lines U87 and U251, were downloaded from three separate datasets using the Gene Expression Omnibus(GEO) database, including GSE 193957(U87), GSE151680(U87 & U251) and GSE100736(U251). Differentially expressed genes(DEGs) were analyzed and obtained from each data set based on the cell line type, using limma and DESeq2 packages. Common DEGs for each cell line were obtained for constructing a protein-protein interaction(PPI) network using the STRING database. Cytoscape software and the cytohubba plugin were used to determine hub genes for common DEGs of each cell line. Then, functional enrichment analyses of hub genes were exerted. Further, RNA sequencing and clinical data of 1018 glioma patients were downloaded from the Chinese glioma genome atlas(CGGA). Univariate Cox analysis was performed for common DEGs of each cell line based on CGGA data and significant genes were extracted for multivariate Cox regression. The “Step” method for each cell line was applied to construct two models based on the common DEGs of U87 and U251 cell lines, and CGGA data. Finally, the risk score based on the last multivariate model, was evaluated for each CGGA patient using this formula: $\Sigma\beta i \times ExpGenei$ (βi was the coefficient value and ExpGenei was the gene expression level). Finally, survival analysis was performed based on the risk scores.

Results: 28 and 24 hub genes were obtained for U87 and U251, respectively. Functional enrichment analyses showed that cell–cell interaction and adhesion could be involved in both U87 and U251 resistance to temozolomide. Two risk score models based on common DEGs, univariate

and multivariate Cox regression for each cell line, were evaluated. Based on the obtained risk scores, patients were bifurcated into “High-risk” and “Low-risk” groups. Survival analyses and Kaplan Meier plots of two models revealed that high-risk patients experience lower survival in comparison to low-risk patients, significantly. Further, it was independent of other variables such as gender, Isodehyrogenase mutation, and grade.

Conclusion: We believe that differential gene expression between resistant and sensitive glioma cells can reveal new genes that could be involved in resistant mechanisms, and could be targeted by future studies. Further, by integrated bioinformatic analyses based on drug resistance, we potentially, demonstrated two models that could predict the survival of glioma patients independent of other variables.

Keywords: Glioma, Drug-resistance, Temozolomide, Brain cancer, U87R, Temozolomide resistance, Differential gen

Identification of Potential Biomarkers Associated with Clear Cell Renal Cell Carcinoma Pathogenesis (Research Paper)

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Introduction: Clear cell renal cell carcinoma is the most frequent subtype of kidney cancer. The need for beneficial biomarkers has become more compelling due to the high mortality of this cancer. We aimed to determine potential biomarkers associated with ccRCC for early diagnosis and treatment.

Methods: The TCGA-KIRC dataset including 72 normal and 542 cancer samples were obtained using TCGAbiolinks package in R programming language and, furthermore, only protein-coding genes were selected by biomaRt package. Expression matrix was normalized through TMM method from edgeR package, and consequently differentially expressed genes (DEGs) with $|log2FC| > 1.5$ and adj P-value < 0.01 were identified. The Gene Oncology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were performed utilizing enrichment tool in Enrichr website, and STRING database was used to establish protein-protein interaction (PPI) network diagram. PPI network was visualized by Cytoscape software and hub genes were calculated by the cytoHubba plugin. Finally, the Gene Expression Profiling Interactive Analysis (GEPIA) database was utilized to perform prognostic value and survival analysis of the hub genes.

Results: Among all 14,656 protein-coding genes, 1,227 DEGs were identified, consisting of 681 down-regulated and 546 up-regulated genes. The results of KEGG pathway analysis demonstrated that the cell adhesion molecules pathway was significantly enriched. In addition, based on GO annotation, DEGs were mainly involved in molecular function of urate transmembrane transporter activity (GO:0015143), cellular component of collagen-containing extracellular matrix (GO:0062023) and biological process of extracellular matrix organization (GO: 0030198). Ultimately, 15 genes with highest maximal clique centrality (MCC) value were regarded as hub genes and according to the survival analysis only 11 of them (UBE2C, HJURP, AURKB, KIF20A, PTTG1, BIRC5, TOP2A, BUB1, CCNA2, CEP55 and TPX2)

which had log-rank test (P<0.01) and HR> 1 were significantly associated with poor prognosis.

Conclusion: The present study illustrated that these 11 detected hub genes: UBE2C, HJURP, AURKB, KIF20A, PTTG1, BIRC5, TOP2A, BUB1, CCNA2, CEP55 and TPX2 may be considered promising biomarkers to improve the poor prognosis of this lethal disease through early diagnosis.

Keywords: ccRCC, Biomarker, Diagnosis, Bioinformatic, TCGA

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Identification of the CBP60g protein orthologue of Arabidopsis thaliana in human genome (Research Paper)

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Introduction: Orthologue identification is a critical aspect of bioinformatics and medical biotechnology that allow inferring gene function, estimating species phylogeny, and constructing phylogenetic profiles. CBP60 protein plays an important role in mediating immune responses and disease resistance in plants. CBP60g lacks the C-terminal CaM interaction, with a N-terminal CaM interaction instead. Previous studies have shown that most of the members of the CBP60 family play roles in pathogen and drought resistance. CBP60g acts synergistically with SARD1 in the pathogen resistance, while antagonistically with CBP60a. In this research, the aim was to identify an Arabidopsis thaliana CBP60 protein orthologue in humans.

Methods: In this research, the CBP60g protein sequences were obtained from the National Center for Biotechnology Information (NCBI) database. Then, to find the orthologue of this protein in humans, the sequence of this protein was analyzed using Ensembl database and BLAST. Furthermore, the physicochemical characteristics of CBP60 protein and its identified orthologue were used from Uniprot and ExPASy databases. In the next step, we used different bioinformatics program to dissect the orthlogue of CBP60g in the human genome.

Results: Through bioinformatics analysis, an orthologue for CBP60 in humans named OPN1MW protein was identified with a similarity percentage of over 60%. The isoelectric point and molecular weight of CBP60g protein are 8.48 and 63067.6 daltons, respectively. The isoelectric point and molecular weight of OPN1MW protein are 8.79 and 40630.40 daltons, orderly.

Conclusion: CBP60g, a member of the CBP60 protein family, interacts with calmodulin and is involved in disease resistance and salicylic acid (SA) accumulation. This interaction highlights the potential role of calmodulin in mediating immune responses in plants. Research conducted to identify a human orthologue for CBP60g, which led to the discovery of its human orthologue, OPN1, is of considerable importance in the field of molecular biology and genetics. Both CBP60g and OPN1MW are involved in biological processes related to immunity and disease resistance. CBP60g is a lipase-like protein that forms complexes with other proteins to regulate immune responses and anthocyanin accumulation in plants. Similarly, OPN1MW is a protein involved in the immune response and disease resistance in humans, suggesting a functional similarity between the two proteins. CBP60g has been identified as a transcriptional activator of immune genes in Arabidopsis thaliana. Understanding the role of CBP60g and its human orthologue, OPN1, in regulating the immune response could provide insight into immune defense mechanisms in plants and potentially in humans. Overall, research conducted to identify CBP60g orthologs in humans and their functional implications in immunity is of great importance in advancing our understanding of molecular processes in plants and humans. It opens avenues for further research and potential applications in various fields including agriculture, medicine and biotechnology.

Keywords: CBP60, Orthologue, OPN1MW, human disease

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Identified hub genes associated with colorectal cancer by Weighted Gene Co-Expression Network Analysis (Review)

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Introduction: Colorectal cancer (CRC) is one of the most common cancers worldwide, with the second highest cancer-related mortality rate. Today, colonoscopy is known to be the gold standard screening method for CRC, but it is an expensive and semi-invasive method. Therefore, patient non-compliance with endoscopy remains a major challenge in this field. On the other hand, the suboptimal accuracy of fecal occult blood testing has led to late diagnosis of CRC. Tumor lymph node metastasis (TNM) stage is currently the basis for CRC prognosis. The significant burden of colorectal cancer and its increasing trend in young adults highlight the need to understand its underlying mechanisms, provide new diagnostic and prognostic markers as well as Improved treatment methods. Weighted gene expression network analysis (WGCNA) is an in silico systems biology tool for analyzing gene expression in a complex network of regulatory genes. This R programming-based tool can identify highly correlated groups of genes (modules) to discover useful hub genes as diagnostic and prognostic biomarkers and therapeutic targets. Thus, this review provide a general overview of hub genes in colorectal cancer that were found by the WGCNA method and as therapeutic and diagnostic targets.

Methods: This is a review study collected from original articles related to the identification of hub genes in colorectal cancer with the keywords “WGCNA” AND “colorectal cancer” AND “hub genes” from 2018 onwards, from Google Scholar and Pubmed, it has been compiled and written. 40 articles were collected and 9 of them were excluded by lack of subject relevance so 31 studies were used. The inclusion criteria were all articles that found hub genes in colorectal cancer using the WGCNA method.

Results: Different studies illustrate that numerous hub genes can be as prognostic biomarkers and therapeutic targets. HCLS1, EVI2B, CD48, GUCA2B, HJURP, CA2, CHP2, SULT1B1, MOGAT2, C1orf115, TDRD5 GPC1, COL6A3, MAL2 , PBXIP1, MPMZ, SCARA3, INA, ILK, MPP2, L1CAM, FLNA, FSTL3, LEMD1 and NKD1 are several hub genes in CRC were identified that have been evaluated with laboratory tests in addition to in silico analysis. The hub genes have been validated only by bioinformatics analysis

include: PAICS, ATR, AASDHPPT, DDX18, NUP107, TOMM6, MT1X, MT1G, MT2A, CXCL8, IL1B, CXCL5, CXCL11, IL10RA, GZMB, KIT, CCNF, DIAPH3, OSBPL3, RERGL, BAI3, CKAP2L, IVL, KRT16, KRT6C, KRT6A, KRT78, SBSN, LMOD3, CDKN2AIPNL, EXO5, ZNF69, BMS1P5, METTL21A, IL17RD, MIGA1, CEP19, FKBP14, CLCA1, GUCA2A, UGT2B17, DSC2, CA1, AQP8, ITLN1, BEST4, KLF4, IQCF6, PAFAH1B1, LMNB1, CACYBP, GLO1, PUM3, POC1A, ASF1B, SDCCAG3, ASNS, PDCD2L, CLCA1, CLCA4, SPARC, DCN, FBN1, WWTR1, TAGLN, DDX28, CSDC2, ABCC13, AMPD1, SCNN1B, TMIGD1, FYN, SEMA3A, AP2M1, L1CAM, NRP1, TLN1, VWF, ITGB3, ILK, ACTN1, COL1A2, THBS2, BGN, COL1A1, TAGLN, DACT3, DKC1, PA2G4, LYAR NOLC1, CCDC69, CLMP, FAM110B, FAM129A, GUCY1B3, PALLD, PLEKHO1, STY11, SOD2, CXCL8, MYL9, CNN1, L12 (RPL12), RPS3A, RPS9, RPL27A, RPL7, RPL28, RPL14, RPS17, mitochondrial ribosomal protein L16, G elongation factor, mitochondrial 2, (ZNF) 813, ZNF426, ZNF611, ZNF320, ZNF573, TIMP1, SPARCL1, MYL9, TPM2, CNN1, AAR2, PSMA7, NELFCD, PIGU, CHEK1, DEPDC1B, FANCI, MCM10, NCAPG, PARPBP, PLK4, RAD51AP1, RFC4.

Conclusion: Advances in high-throughput techniques and analytical methods such as WGCNA have provided new opportunities to study CRC at different molecular levels and advance our knowledge of CRC, ultimately leading to generate significant amounts of data. CRC is a very complex disease and thousands of molecules are changed during the process. Among these molecules, some may be valuable markers for cancer diagnosis and prognosis. These dysregulated molecules could serve as potential targets to help scientists develop new targeted drugs to treat CRC.

Keywords: WGCNA, colorectal cancer, hub genes, biomarker

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Immune Checkpoint Inhibitor-Related Post-Immunotherapy Arthritis: Mechanisms, Manifestations, and Management Strategies (Review)

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Introduction: Immune checkpoint inhibitors (ICIs) are cutting-edge therapeutic approaches in clinical oncology that have transformed the cancer treatment landscape by unleashing the immune system's potential to attack tumoral cells. Nonetheless, this enhanced immune activation can also lead to various immune-related adverse events (irAEs). Post-immunotherapy arthritis (PIA), primarily associated with ICIs, presents a clinical challenge, demanding a multidisciplinary approach to diagnosis and management. This review delves into the mechanisms, clinical manifestations, and management strategies for post-immunotherapy and ICI-related arthritis.

Methods: A comprehensive literature review was performed using Medline (via PubMed) and Scopus databases, Google Scholar search engine, and ClinicalTrials.gov registry of clinical trials in August 2023. Relevant studies, discussing the mechanisms, manifestations, and management of post-immunotherapy and ICI-related arthritis were reviewed critically, regardless of the cancer type and population.

Results: PIA is seen in both PD-1/PD-L1 and CTLA-4-targeting monotherapy and ICI combination therapy strategies. The precise mechanisms of PIA are not fully elucidated. However, several hypotheses have been proposed so far, including dysregulated immune response by disrupting the balance of pro-inflammatory and regulatory immune responses, molecular mimicry as activated T cells potentially cross-react with the autoantigens expressed in joint tissues, and alterations in regulatory T cells (Tregs), which ultimately affects the immune tolerance and could lead to unchecked activation of autoreactive T cells. ICI-related PIA is presented with a variety of manifestations, ranging from mild arthralgias to severe polyarthritis, typically from weeks to months after the initiation of treatment. The most commonly affected joints are the knees, wrists, and small hand joints. Morning stiffness, joint swelling, and pain are hallmark features. Meanwhile, metastasis and infection could also present with the same initial symptoms. Laboratory evaluation often reveals elevated inflammatory markers, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Rheumatoid factor (RF) may be positive in a subset of patients, resembling seropositive

rheumatoid arthritis. However, seronegative cases have been commonly observed in the studies. Management of PIA requires a collaborative effort to maintain the efficacy of the cancer treatment. Nonsteroidal anti-inflammatory drugs (NSAIDs) can provide symptomatic relief for mild cases but should be used with caution, as they are associated with many gastrointestinal and renal adverse events. Systemic corticosteroids, such as prednisone, are often required to control moderate to severe PIA. Still, long-term use of systemic corticosteroids is not generally recommended and requires further studies. Disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, could be considered for refractory cases. DMARD-resistant cases might benefit from cytokine-targeting biological agents, which are still under investigation in the context of cancer treatment irAEs. Finally, similar to other irAEs, temporary discontinuation of ICIs may be necessary in cases of severe arthritis.

Conclusion: PIA is an emerging challenge in cancer immunotherapy. Understanding the underlying mechanisms, presenting manifestations, and clinical management strategies could direct a collaborative approach to effective management of this cancer treatment complication. Future studies should provide in-depth insight into potential prognostic and early-diagnostic biomarkers for ICI-related PIA. Additionally, the development of novel therapies with a more favorable safety profile is a priority approaching the irAEs.

Keywords: Adverse events, Arthritis, Cancer immunotherapy, Immune checkpoint inhibitor, Inflammation

Immunoinformatic design of a novel epitope-based vaccine against Canine monocytic ehrlichiosis (Research Paper)

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Introduction: Canine monocytic ehrlichiosis is an emerging tick-borne disease among dogs around the world, including Iran. It is caused by infection of monocytes/macrophages with a bacterium called Ehrlichia chaffeensis. This obligate intracellular Gram-negative bacterium can enter the white blood cells where it reproduces and infect the lymph nodes, spleen, liver and bone marrow. The chronic phase of the illness can lead to pancytopenia (very low blood cell counts), bleeding, lameness, neurological and ophthalmic disorders, and kidney disease and even death. So far, Treatment options are limited to the broad-spectrum antibiotic doxycycline and no vaccine is currently available. The best strategy for managing the disease is to interrupt the cycle of infection by directing the immune responses toward key virulence factors as potential targets by vaccination. Genomic and proteomic data relevant to the living organism immune systems and diseases and wide variety of bioinformatics tools have given rise to the field known as immunoinformatics, and in particular reverse vaccinology approach. This method is useful in the development of multi-epitope vaccine which is generally considered to be safe in comparison to conventional vaccine design approaches such as attenuated or subunit vaccines that have high risk of toxicity and autoimmunity. Our study aimed to design a vaccine construct against E. chaffeensis based on reverse vaccinology for the first time.

Methods: In this study, OMP-1B which is a major outer membrane protein in E. chaffeensis was selected as an antigen to obtain epitopes. Antigenicity of the selected antigen was predicted by the VaxiJen v2.0 server and the default threshold of 0.5 for bacteria was maintained. Prediction of B-cell and T-cell epitopes from selected target proteins is done through ABCpred and IEDB MHC I binding tool online servers. For quality prediction of formation of MHC-epitope complex structures GalaxyPepDock server was employed to perform docking of DLA-8803401, DLA-8850101, and DLA-8850801 with CTLs. Furthermore, the potent epitopes were screened on the basis of antigenicity, and toxicity, as evaluated by VaxiJen v2.0 and ToxinPred servers. The predicted antigenic epitopes were linked together and then fused to Beta-defensin as adjuvant to enhance immunogenicity of the vaccine. It linked by the “EAAAK” linker followed by CTL epitopes which were linked together by

the “AYY” linkers. Further, the B cell epitopes were linked by KK linkers. The ProtParam server was used to determine the physical and chemical characteristics of the final vaccine. I-TASSER server was used to generate the 3D model of linear vaccine construct. Then, the refinement of 3D structure model was done using GalaxyRefine Server. The tertiary structure was validated using ERRAT score followed by ProSA-web analysis. Further, the overall quality of the generated model of vaccine was determined by Ramachandran plot analysis using Procheck server. Also, interactions of the vaccine with TLR5 is studied as it induce immune response when activated by the vaccine. FTsite server was utilized for predicting the active residues for the interactions. The docking of was performed by HADDOCK 2.4. The best cluster was chosen from the docked clusters based on lowest HADDOCK score. HADDOCK Refinement Interface was used to refine the chosen cluster. The best structure after refinement was chosen and their binding affinity was calculated using PRODIGY web server. Then, the interacting residues between the vaccine and the TLR5 was mapped using PDBsum. Finally, the recombinant plasmid was designed by inserting the adapted codon sequence into pET-28a (+) vector using SnapGene software.

Results: Through epitope mapping 8 T-cell and 5 B-cell were predicted and fused together. Further analysis showed that the constructed vaccine was highly antigenic, and non-toxic with a molecular mass of 35.3kDa. The 3D model depicted that 82.8% of residues are in favorable region, 13.5% of residues in allowed region and 3.7% in outer region according to Ramachandran plot analysis. Further analyses by ProSA revealed Z- score is - 1. Moreover, the refined model score was 51.4 in quality check analysis through ERRAT. All these results showed that the refined model have good quality. Also, the results of docking demonstrated that the vaccine is potentially able to interact with TLR5 and is energetically feasible.

Conclusion: Overall, the designed vaccine holds promise as a potential preventive approach for Canine monocytic ehrlichiosis.

Keywords: epitope-based vaccine, Canine ehrlichiosis

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Immunomodulation methods in tissue engineering (Review)

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Introduction: Immunomodulation methods play a vital role in tissue engineering, as they help overcome immune responses that can hinder the success of tissue grafts and implants. By manipulating the immune system's response, tissue engineers aim to enhance the integration, function, and longevity of engineered tissues. This abstract explores various immunomodulation strategies employed in tissue engineering and their impact on tissue graft acceptance and long-term outcomes. It also highlights the challenges and future directions in this rapidly evolving field.

Methods: This review was prepared by searching Science Direct, Google Scholar, Pub-Med, Scopus, and Web of Science databases.

Results: One approach to immunomodulation involves the use of biomaterials and scaffolds with controlled release systems. These systems can deliver immunomodulatory agents, such as anti-inflammatory drugs or growth factors, to regulate immune cell behavior at the implant site. Additionally, surface modifications of biomaterials can play a crucial role in modulating local immune responses. For instance, modifying the surface chemistry or topography can influence macrophage polarization and adhesion, promoting a favorable environment for tissue integration. Another promising strategy is the incorporation of immunosuppressive cells, such as regulatory T cells or mesenchymal stem cells (MSCs), into engineered tissues. These cells actively suppress the immune response, creating an immunosuppressive microenvironment around the graft. MSCs, in particular,

have shown great potential due to their immunomodulatory properties, which include modulating T cell activity, promoting tissue repair, and secreting anti-inflammatory factors. Furthermore, tissue engineering approaches that incorporate decellularization and recellularization techniques can minimize immunogenicity. Decellularization involves removing cellular components from a donor tissue while preserving the extracellular matrix (ECM), allowing for repopulation by patient-specific cells. This method helps reduce the immune response against the graft. Molecular interventions offer a precise approach, utilizing techniques such as gene editing or RNA interference to modulate the immune response. Recent advancements in CRISPR-Cas9 technology have enabled the development of immune-evasive grafts by editing specific genes responsible for antigen presentation. However, challenges remain in developing optimal immunomodulation strategies. Achieving a delicate balance between immune suppression and host defense is crucial, as excessive immunosuppression may lead to infection or tumor growth. Additionally, the long-term stability and functionality of engineered tissues still need to be addressed.

Conclusion: Immunomodulation methods in tissue engineering hold great promise for improving tissue graft acceptance and integration. By leveraging biomaterials, controlled release systems, immunosuppressive cells, decellularization techniques and molecular interventions, researchers are progressing toward creating immunologically stable and functional tissues and organs.

Keywords: Immunomodulation, Tissue Engineering, Biomaterials, Scaffolds, Decellularization

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Immunopathology of Inflammatory Bowel Disease and The Role of Toll-like Receptors Therein (Review)

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract, which mainly includes Crohn's disease and ulcerative colitis. Ulcerative colitis is limited to the large intestine, which can lead to ulceration and bleeding; But Crohn's disease can affect any part of the digestive system and can lead to abscesses and abdominal pain. The pathophysiology of inflammatory bowel disease includes genetic, environmental, epithelial, microbial, and immunological factors. Several evidences suggest that IBD results from a dysregulation of the immune response to symbiotic organisms. One of the main factors in the pathogenesis of IBD is immune system disorders. Different components of the mucosal immune system are involved in the pathogenesis of IBD. The clearest example is the intestinal immune system, which must establish the required balance between the immune response to symbiotic bacteria and pathogenic bacteria. Various studies have shown that epithelial barrier function, immune system, and regulation of immune response are known as key elements of intestinal homeostasis so disruption in these can lead to IBD. Epithelial cells secrete Mucin and Defensin to protect themselves against the invasion of bacteria and other invading agents. Mucin is a glycoprotein that prevents bacteria from coming into contact with digestive cells by forming an adhesive physical barrier. In addition to mucin, an antimicrobial peptide called defensin is also secreted by digestive epithelial cells, which has a protective function against luminal bacteria, and a defect in their production allow pathogenic bacteria to invade epithelial cells and cause intestinal inflammation. However according to a series of other studies, both innate and adaptive immune systems are involved in the occurrence of IBD. Toll-like receptors (TLRs) are a family of pattern recognition receptors that are found on cell surfaces and intracellular membranes that as a member of innate immunity play an important role in identifying pathogens, maintaining intestinal homeostasis, controlling immune responses, and shaping the microbiota. TLRs have been

identified in both intestinal epithelial cells and gastrointestinal stromal tissue cells. Expression of TLR in the epithelium of the gastrointestinal tract varies from person to person. For example, the expression of TLR2, 4, 8, and 9 genes increases in patients with ulcerative colitis, while TLR5 is upregulated in active ulcerative colitis and downregulated in inactive ulcerative colitis. In fact, the activation of TLR signaling induces the stimulation of inflammatory cytokines which may be a precursor to the onset of inflammatory diseases such as IBD. Further studies have also demonstrated that TLR4 can cause tissue destruction and ulceration in the intestine. TLR3 is significantly reduced in epithelial cells of patients with active IBD. Based on their research, a team of scientists identified TLR6 as the trigger for experimental colitis. Furthermore, based on other findings, TLR6 was introduced as a potential target for the treatment of IBD. As a result, each member of the TLR family and its subsets plays both positive and negative roles in the emergence of IBD.

Methods: Various experiments have been conducted by scientists to study the positive and negative roles of TLRs and their subsets in IBD.

Results: In various trials, TLRs and their activators have been found to have significant positive and negative effects on IBD. Interleukins and Interferons are known to be effective cytokines in TLR activity. For instance, in one experiment, IFN-β was found to induce a positive clinical response and remission in a large number of patients with ulcerative colitis by modulating innate immune system function and regulate macrophage and dendritic cells function. In a series of studies, TLR4 has been shown to have a dual role in IBD. As it can maintain the integrity of the intestinal lining and prevent the entry of harmful bacteria, it can also cause the destruction of tissues and wounds. It has been confirmed that stimulated intestinal glial cells can release and activate inflammatory cytokines by releasing nitric oxide, leading to exacerbation of intestinal inflammation.

Conclusion: More research is needed on IBD. Further research into the role of the immune system and the interaction of various immune components with the microbiota may open new horizons for further identification of IBD.

Keywords: Inflammatory Bowel Disease, Innate Immunity, Ulcerative Colitis

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Impact of epigenetic modifications on male fertility (Review)

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Introduction: Infertility is the inability to achieve pregnancy after 12 or more months of regular and unprotected intercourse as defined by the World Health Organization (WHO). Male infertility is a complex disease caused by anatomical defects, injuries, endocrine disorders, immune system problems, genetic factors, and viruses. There are over 48.5 million couples worldwide who suffer from infertility. Additionally, it is estimated that there are more than 30 million infertile men globally. Despite the alarming prevalence, the causes of male infertility remain enigmatic in a large percentage of cases, this is why researchers have recently tried to study the epigenetic origin of male infertility. Epigenetic research focuses on changes in gene expression inherited through meiosis or mitosis without altering the DNA sequence. These modifications include histone modifications (a post-translational modification in histones that is very important in the proper functioning of cells. The N-terminal contains amino acids that can be used for methylation, acetylation, phosphorylation, and ubiquitylation of the receptor), DNA methylation (an essential epigenetic modification specifically related to gene silencing), chromatin remodeling, and RNA-based mechanisms (we can refer to changes in miRNA, mRNA, and piRNA).

Methods: In this review study, we analyzed articles related to male infertility from 2015 to 2023 using keywords such as epigenomics, DNA methylation, and chromatin rearrangement, obtained from the PubMed and Google Scholar databases.

Results: Recent studies suggest a link between male infertility and methylation modifications. Specifically, MTHFR is the most crucial gene in the methylation process. Numerous studies show that hypermethylation in the promoter of this gene is associated with idiopathic male infertility. It has been reported that hypermethylation of the promoter region of SFN and PAX8 genes can result in weak parameters in human semen. However, if the same genes are hypermethylated, it can lead to low sperm concentration in semen. This process negatively affects the morphology and motility of sperm. LIT1 promoter hypermethylation is associated with poor sperm parameters in humans. Additionally, infertile individuals have a distinct methylation pattern of

CpG islands in this gene. NTF3 hypermethylation is linked to low sperm concentration, morphology, and motility. Increased methylation is associated with decreased semen quality in CREM, DAZL, and RHOX genes. Meanwhile, the H19 gene is linked to male infertility when its methylation is reduced also H19/IGF2 gene expression may influence human fertility. The studies on the relationship between chromatin changes and male infertility indicate that protamines are phosphorylated before binding to DNA and dephosphorylated during nucleoprotamine maturation. Camk4 is a protein that is responsible for phosphorylating protamine type II. Mutations in this protein can lead to infertility and defective spermatogenesis in men. Since type 1 and type 2, protamines are vital for sperm function, the semi-insufficient state of these two genes makes the chromatin structure abnormal, and DNA is damaged resulting in infertility. Research has also shown that the proportion of protamine type 1 to type 2 is a significant factor in this process. These deviations also can affect semen quality, reducing sperm concentration and changing movement and morphology. They also impact DNA stability. Research has shown that individuals with low sperm motility have lower levels of mRNA BDNF compared to those with normal sperm production. A protein called GP130 is also involved in sperm motility and has been found to have high levels of mRNA in men with very low sperm motility. In people with oligospermia, low levels of DDX4 and VAS transcripts, which are essential for sex line development, have been reported.

Conclusion: Diagnosing the cause of male infertility and available treatments currently do not provide a solution for all cases. Epigenetic factors play a role in this type of infertility and should be considered when examining infertile individuals. Correcting these factors is easier than correcting genetics due to the dynamics of the epigenetic pattern. Researching these factors shortly will allow for the development of epidurals to correct epigenetic processes and improve fertility in individuals.

Keywords: male infertility, epigenetic, methylation modifications, chromatin rearrangement

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Impact of Exercise on Gut Microbiome: Age and BMI-Dependent Variations in Interventional Studies (Review)

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Introduction: The gut microbiota, comprising a diverse community of microorganisms in the digestive system, plays a pivotal role in maintaining health. Emerging evidence suggests that exercise training programs can modify the composition and function of the gut microbiota, potentially countering dysbiosis and the effects of chronic metabolic conditions, and even aging. This review study investigates the impact of exercise on the gut microbiome, taking into account age and body mass index (BMI) variations among participants.

Methods: Since active individuals and professional athletes tend to eat differently from sedentary individuals and have altered gut microbial metabolic pathways, only longitudinal studies on sedentary individuals were included to investigate the causality of this association. Moreover, exercise effect on gut microbiota can be immediate (acute physiological response) or delayed; the later which is referred to as training-effect was explored in this review. Articles were excluded if the participants were receiving medications, supplements, or specific diets designed to, or with the potential to alter the gut microbiota community. A systematic search of published peer-reviewed articles on PubMed and Google Scholar were conducted. Data from selected studies were meticulously extracted and recorded in an Excel file.

Results: The current review included 18 original studies meeting the inclusion criteria, revealing diverse efficacy levels and considerable inter-individual variations. Notable findings include: In obese children, exercise significantly improved gut microbiome composition toward a healthier composition. However, exercise did not induce significant changes in the gut microbiome of normal-weight adolescents. In obese or insulin resistant adults, Bacteriodetes phylum increased significantly after exercise interventions. Lean adults exhibited an increase in the Firmicutes to Bacteroidetes (F/B) ratio, while obese subjects displayed the opposite trend. In the elderly group, studies with lean subjects reported a significant decrease in Clostridium abundance after exercise intervention. Studies with a wide range of BMI in both adults and elderly, as well as one study in adolescents who recruited participants with

different baseline physical activity levels, did not report significant alterations in gut microbiome composition.

Conclusion: The observed differences in baseline gut microbiome composition among lean, overweight, and obese individuals highlight the need for targeted interventions. This review underscores the importance of considering participants' baseline BMI, physical activity levels, and metabolic condition when investigating the impact of exercise on the gut microbiome. Future studies should address baseline microbiota heterogeneity and strive to minimize it, either by focusing on a narrow range of BMI or by adjusting results for influential factors.

Keywords: Gut microbiome, Exercise, Body mass index, age

Importance study effect natural killer (NK) cell therapy, hematopoietic stem cell transplantation for leukemia (Review)

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Introduction: Natural killer (NK) cells belong to innate lymphoid immune cells that contribute to antitumor responses without prior sensitization. Dealing to the currently applied innate lymphoid cell nomenclature, NK cells are a prototypical member of the group 1 innate lymphoid cells insofar as they produce interferon g(IFN_γ) and developmentally require the common cytokine receptor g chain the transcriptional repressor inhibitor of DNA binding 2, and t bet. Allogeneic hematopoietic stem cell transplantation (HSCT) transplantation has a major role in the treatment of leukemia and hematological disease often the only treatment providing a change of cure in other wise refractory diseases. The primary approaches involved total body irradiation (TBI) or cyclophosphamide (CY).

Methods: we reviewed about 22 articles were conducted from 2019 to 2023 in the world and Iran. We searched some key words such as natural killer, stem cell, hematopoietic, leukemia, acute amyloid leukemia in ScienceDirect, Elsevier, PubMed and SID.

Results: NK cells use different innated receptors to sense their environment and respond to alterations induced by infections or by malignant cells transformation. In a process termed licensing NK cells use iKIRs for self-major histocompatibility complex (MHC) class I molecules to maintain a state of responsiveness and to kill target cells have lost MHC class I. Human NK cells comprise two main phenotypes based on the CD56 and CD16 markers. The CD56dim CD16+NK subset has great cytotoxic potential and is predominant in blood, whereas the CD56high CD16- subset produces abundant cytokines and is more abundant in lymph nodes. The functionality of NK cells is mediated and controlled by the balance between the expression of activating are inhibitory receptors. The main activating receptors are natural cytotoxic receptors (NCR, NKP30, NKP46, NKP44) NKG2D and DNAM-1 whereas the killer immunoglobulin like receptor (KIR) family and NKG2A are inhibitory receptors. In a high percentage of AML patient, the expression levels of some activating receptors (NKG2D, NKP30, NKP46, DNAM-1) are null or very low. Fauriat et all, reported that the NKP30 and NKP46 expression is reduced in

AML patients at diagnosis but is partially recovered after CR and decreases again in an episode of disease relapse. It is also clear established that high levels of expression of NKP30 and NKP46 are associated with higher rates of overall relapse free and progression free survival compared with patient with reduced expression of their receptors. One benefit of this therapy is the low incidence of graft versus host disease (GVHD) and the production of a strong graft versus leukemia (GVL) that is associated with better survival and lower probability of relapse. Ex vivo stimulation of NK with a cytokine cocktail of IL12, IL15 and IL18 is an established alternative to avoid the in vivo administration of IL2 after NK cell infusion. These cells known as CIML (cytokine induced memory like) proliferate and produce high levels of IFN_γ during the first week after which its production decreases. Relapse of residual disease is a common cause of reduced survival following HSCT. This occurs in 20_70% of patients and is dependent on several factors including pre transplant disease status, cytogenetic subtypes (in acute myeloid leukemia (AML)) and in acute lymphoid leukemia (ALL), stem cell source, age of the patient and donor and type of conditioning regimen. In addition, relapse contributes to 40-45% of deaths following HLA matched identical HSCT and 34% in unrelated donor HSCT. The use of reduced intensity conditioning regimens has also led to GVL effects, which have been most marked in chronic myeloid leukemia (CML) and are also detectable myelodysplastic syndrome (MDS), AML and ALL.

Conclusion: NK cells and established NK cell lines such as NK92 can also be redirected towards target antigens expressed on leukemia blasts by chimeric antigen receptors (CARs). It has been shown that CAR_NK cells can overcome inhibitory signals and induce specificity killing of leukemia cells. In CML long term remissions can readily be obtained by the treatment with low dose IFN_γ and DLI, in AML long term remission may be obtained by a more aggressive approach involving mobilized stem cells and GM_CSF following cytarabine of repeated treatments with targeted drugs like azacytidine, sorafenib, midostaurin, immune modulatory, blast modulatory kit and DLI.

Keywords: natural killer, stem cell, hematopoietic, leukemia, acute myeloid leukemia

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Improved TRAIL Efficiency by Mitoxantrone loaded PLGA Nanoparticles in Glioblastoma Cancer Cell (Research Paper)

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Introduction: Glioblastoma (GBM) is one of the aggressive and lethal form of brain tumors, with a high degree of invasion. Drug resistance of tumor cells is one of important reasons that prevents the success of therapeutic strategies. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), is a type-II transmembrane protein belongs to the tumor necrosis factor (TNF) superfamily wich induces apoptosis in different tumor cells but not in most normal cells. Nevertheless, there are some limitation in TRAIL clinical application because of its short biological half-life and TRAIL resistance mechanisms. On the other hand, combination therapy is known as a possible solution for many drug resistances. Mitoxantrone (MTX) as an efficient anti-neoplastic drug has been prescribed against malignant glial cells and has been classified as a BCS-IV (low solubility/low permeability). Myelosuppression, neuropathy and nephrotoxicity have been reported as the important side effects of MTX. Therefore, a novel drug delivery system for MTX could be promising to reduce its adverse effects and fix the low solubility. So, in the current study, a system comprising of Poly (lactic-co-glycolic acid) (PLGA) nanoparticles loaded with MTX along with TRAIL plasmid delivery to glioblastoma cancer cells was designed and increase in their sensitivity was investigated.

Methods: PLGA nanoparticles containing MTX were fabricated using a water-in-oil-in-water (W/O/W) double emulsification and solvent evaporation method and characterized. Synergistic effect of PLGA-MTX and TRAIL plasmid

delivery to cancer cells was evaluated by both MTT and annexin V-FITC/PI investigation against GL-261 cancer cell line.

Results: Significant more cytotoxic effect on GL-261 cells was acquired with combination treatment of PLGA-MTX nanoparticles and TRAIL plasmid, consequently cell viability of this treatment was 16% compared to 38% for MTX-PLGA alone and 87% for TRAIL alone treatments.

Conclusion: It concluded that PLGA-MTX can be remarked as a potential agent for sensitizing glioblastoma cancer cells to TRAIL. However, further studies are necessary for its clinical applications.

Keywords: Glioblastoma, TRAIL, Mitoxantrone · PLGA.

Improvement of ovarian tissue in rats with polycystic ovary syndrome treated with the anti diabetic drug Empagliflozin (Research Paper)

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Introduction: Polycystic ovary syndrome (PCOS) is one of the endocrine disorders in women of reproductive age, which has no specific treatment due to its multifactorial nature. Therefore, it is important to provide new treatment solutions. Considering the incidence of insulin resistance and blood glucose increase in polycystic ovary syndrome on one hand and the anti-diabetic properties of empagliflozin on the other hand, the effect of this drug in the treatment of PCOS complications was investigated.

Methods: Forty female rats (Wistar) with 200-220g weight were selected and divided into 5 equal groups. All rats, except the control group (healthy rats), became PCOS with daily oral administration of 1 mg/kg/bw of letrozole solution. Then they were divided into Control groups (healthy rats), Sham 1 (PCO without treatment), Sham 2 (PCOS rats treated with 500mg/kg/bw metformin), and two groups treated with doses of 30 and 50 (mg/kg/bw) of Empagliflozin solution. After 60 days of treatment, according to the principles of working with animals, all rats were anesthetized and blood was taken from them. Immediately, the ovarian tissue was removed from the body, fixed in a 7% formalin solution, and transferred to the laboratory to prepare tissue sections by the standard stereological method. The slides were prepared and photographed with a microscope equipped with a camera. The thickness of the theca, the diameter of the ovum, and the corpus luteum were measured using Streolite software, and the number of follicles was counted. The resulting data (Mean ± SD) were analyzed with SPSS version 20 software and ANOVA, and the groups were compared with Tukey tests.

Results: The findings of this research showed that the use of metformin and empagliflozin in treated groups decrease blood glucose, body mass, luteinizing hormone, and testosterone, and increase follicle stimulating hormone and progesterone in comparison to PCO rats without treatment (Sham 1) significantly ($p<0.5$). Also, the adverse changes in ovarian tissue caused by PCO induction include a decrease in the diameter and number of

corpus luteum, a decrease in the diameter of the ovum, the occupation of a larger volume of the ovary by cystic and atretic follicles, and a greater thickness of the theca, were improved especially in rats consuming a higher dose of empagliflozin. The results showed a significant increase in the average number of single-layered follicles and a significant decrease in the number of antral follicles and Graafian follicles in the PCO group compared to the control group, which was significantly compensated in the groups taking metformin and especially the higher dose of empagliflozin. They reached the level of the Control group. The mean number of primary follicles was not significantly different between the studied groups, but there was a significant decrease in the mean of corpus luteum in the PCO group compared to the control group ($p<0.001$), it was adjusted by taking both drugs. Cystic and atretic follicles were reduced by treatment with metformin, and empagliflozin especially at higher doses ($p<0.001$) and ($p<0.001$) in the treated groups.

Conclusion: Empagliflozin has significantly improved the adverse changes caused by PCOS in ovarian tissue and the number of follicles with a similar effect to metformin. The more effect of the higher dose of empagliflozin compared to a lower dose and metformin shows the dependence of the drug effect on the appropriate dose. With more research on this drug, it may be a good option in the treatment of PCOS.

Keywords: Empagliflozin, Body mass, Follicle graph, Blood sugar, Theca

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Improvement the expression and purification of PvpA-pMGA1.2 protein from Mycoplasma gallisepticum. (Research Paper)

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Introduction: Introduction: Mycoplasma gallisepticum is a causative agent of chronic respiratory disease in chickens, typically causing great economic losses. pMGA and pvpA genes encode major surface proteins in M. gallisepticum containing pathogenic, antigenic, and immune evasion characteristics. This study aims is to obtain the optimum conditions for high expression and purification of PvpA-pMGA1.2 recombinant protein from Mycoplasma gallisepticum.

Methods: Methods: The PvpA-pMGA1.2 gene was cloned into a pET-32a (+) expression vector. BL21(DE3) was used as expression host for transformation.The expression conditions optimized then by adjusting parameters such as culture media, induction time, temperature, and IPTG concentration.

Results: Results: SDS-PAGE analysis showed that the production of rPvpA-pMGA protein was at the highest level when post induction incubation, IPTG concentration, and duration of induction were 37ºC, 0.1M and 16h in 2xTY medium respectively. The purification of the rPvpA-pMGA protein under native conditions using Ni-NTA pull-down was optimum in one hour binding process at 37°C, three times washing process and elution buffer with a pH 8.

Conclusion: Conclusion: Based on the results of this study, optimizing the expression and purification process for over production of rPvpA-pMGA protein resulted in the large quantity of pure recombinant antigen that forms the basis for future investigation on the design of rapid diagnostic tests and more effective subunit vaccine candidates for avian mycoplasmosis.

Keywords: Key words: Mycoplasma gallisepticum, rPvpA-pMGA1.2, Recombinant protein

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In search of subcortical and cortical morphologic alterations of a normal brain through aging: an investigation by CT scan (Research Paper)

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Introduction: Morphologic changes in the brain through aging, as a physiologic process, may involve a wide range of variables including ventricular dilation, and sulcus widening. This study reports normal ranges of these changes as standard criteria.

Methods: Normal brain CT scans of 400 patients (200 males, 200 females) in every decade of life (20 groups each containing 20 participants) were investigated for subcortical/cortical atrophy (bicaudate width (BCW), third ventricle width (ThVW), maximum length of lateral ventricle at cella media (MLCM), bicaudate index (BCI), third ventricle index (ThVI), and cella media index 3 (CMI3), interhemispheric sulcus width (IHSW), right hemisphere sulci diameter (RHSD), and left hemisphere sulci diameter (LHSD)), ventricular symmetry. Distribution and correlation of all the variables were demonstrated with age and a multiple linear regression model was reported for age prediction.

Results: Among the various parameters of subcortical atrophy, BCW, ThVW, MLCM, and the corresponding indices of BCI, ThVI, and CMI3 demonstrated a significant correlation with age ($R2 \geq 0.62$). All the cortical atrophy parameters including IHSW, RHSD, and LHSD demonstrated a significant correlation with age ($R2 \geq 0.63$).

Conclusion: This study is a thorough investigation of variables in a normal brain which can be affected by aging disclosing normal ranges of variables including major ventricular variables, derived ventricular indices, lateral ventricles asymmetry, cortical atrophy, in every decade of life introducing BW, ThVW, MLCM, BCI, ThVI, CMI3 as most significant ventricular parameters,

and IHSW, RHSD, LHSD as significant cortical parameters associated with age.

Keywords: brain, computed tomography, aging, ventricular system

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In silico analyses for potential key genes associated with colon cancer (Research Paper)

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Introduction: colorectal cancer(CRC) is one of the most prevalent cancers in the world, With between one and two million new cases being diagnosed each year. It is also the fourth most common cause of cancer-related death. Effective methods to diagnose and treat cancer may result from comprehending hub genes involved in colorectal cancer (CC) metastasis. In this study, we aim to identify the colorectal cancer's key genes and look into their underlying molecular mechanisms.

Methods: In the current study, two microarray dataset (GSE103512, GSE77167, GSE74604) were downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with $|FC| > 1$ and P-value < 0.05 were considered to be significant. The Venn diagram was carried out for the overlapped part via Funrich software.

Results: A total of 7 overlapped upregulated genes and 4 downregulated genes were identified. Analysis showed that up-regulated genes involve in the metabolism of lipids and lipoproteins, cholesterol biosynthesis I, mesenchymal-to-epithelial transition. Down-regulated genes mainly associate with alpha4 beta1 integrin signaling events, Integrin family cell surface interactions, beta1 integrin cell surface interactions and p53 pathway.

Conclusion: Our study suggests that HLA-DPA1, FCMR, ADAM28 , ANKRD22, ANXA3, DHCR7, CEP55, S100P and ANLN may be potential biomarkers and therapeutic targets for CC.

Keywords: colon cancer, key genes, Microarray analysis

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In Silico Analysis of Glutaminyl Cyclase Gene (QPCT) gene Expression Change Associated with Stages in Pancreatic Adenocarcinoma (Research Paper)

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Introduction: Pancreatic adenocarcinoma (PAAD), the most common form of pancreatic cancer, is characterized by its aggressive nature and poor prognosis. This malignancy arises from the cells lining the pancreatic ducts and poses significant challenges in terms of diagnosis and treatment. Although many genes have been implicated in its pathogenesis, the expression changes of the Glutaminyl Cyclase Gene (QPCT) in PAAD have been less investigated. Therefore, we conducted a study to investigate the role of QPCT in pancreatic adenocarcinoma and its potential as a diagnostic and prognostic biomarker.

Methods: In this Descriptive-analytical study, we used TCGA data from the OncoDB database to evaluate changes in the QPCT gene expression in PAAD to explore abnormal patterns in gene expression related to clinical data that were identified. Gene expression was normalized by the TMP method, and the groups were compared based on cancer and normal samples. Criteria for including patient data in the present study are demographic information such as pathological stage, especially T-stage.

Results: The TCGA pancreatic adenocarcinoma dataset consists of 178 normal and 200 cases of PAAD tissue samples. Moreover, the expression level of QPC was significantly increased in samples with TNM status Tstage4 compared to Tstage1, Tstage2, and Tstage3. Additionally, our Kaplan-Meier analysis indicated that the increase in QPC expression was associated with poor prognosis of patients (Rank=0.03). Finally, we used ROC analysis to show that QPC can be considered a potential diagnostic biomarker (AUC=0.99, P<0.001).

Conclusion: Our study demonstrates that the expression level of QPCT is increased in PAAD and is associated with a poor prognosis in patients. Furthermore, we suggest that QPCT expression can be used as a diagnostic and prognostic biomarker for the targeted treatment of patients with PAAD.

Our findings provide new insights into the pathophysiology of this disease and may help improve patient outcomes through early detection and personalized treatment.

Keywords: Biomarker, Pancreatic Adenocarcinoma, Gene expression, T-stage, QPCT gene

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In Silico Analysis of Glutaminyl-Peptide Cyclotransferase (QPCT) Gene Expression Changes Associated with Tumor Progression stages in Pancreatic Adenocarcinoma (Research Paper)

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2. Department of Biology, East Tehran Branch, Islamic Azad University, Tehran, Iran

Introduction: Pancreatic adenocarcinoma (PAAD), the most common form of pancreatic cancer, is characterized by its aggressive nature and poor prognosis. This malignancy arises from the cells lining the pancreatic ducts and poses significant challenges in diagnosis and treatment. Although many genes have been implicated in its pathogenesis, the expression changes of the Glutaminyl-Peptide Cyclotransferase (QPCT) gene in PAAD have been less investigated. Therefore, we conducted a study to examine the role of the QPCT gene in pancreatic adenocarcinoma and its potential as a diagnostic and prognostic biomarker.

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Conclusion: Our study demonstrates that the expression level of the QPCT gene is increased in PAAD and is associated with a poor prognosis in patients. Furthermore, we suggest that QPCT gene expression can be used as a diagnostic and prognostic biomarker for the targeted treatment of

patients with PAAD. Our findings provide new insights into the pathophysiology of this disease and may help improve patient outcomes through early detection and personalized treatment.

Keywords: Biomarker, Pancreatic Adenocarcinoma, Gene expression, T-stage, QPCT gene

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In silico analysis of the second and third structure of the Calmodulin-binding Protein 60 g (CBP60g) Cucumber mosaic virus (Research Paper)

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Introduction: In nature, plants are frequently exposed to drought and bacterial pathogens simultaneously. Calmodulin-binding Protein 60 g (CBP60g) is transcription factor. under combined stress, drought through the ABA pathway downregulates the induction of Calmodulin-binding Protein 60 g (CBP60g) and Systemic Acquired Resistance Deficient 1 (SARD1), two transcription factors crucial for SA production upon bacterial infection. Due to the important role of CBP60g, it is important to investigate the secondary and tertiary structure of this receptor. Predicting of the secondary and tertiary structure of proteins is very important in subsequent protein studies and the study and identification of the function of unknown proteins. Predicting the tertiary structure of proteins can also be used in molecular docking.

Methods: In this study, the Phyre2 software was used to investigate the secondary structure of the CBP60g protein. Three-dimensional structure modeling was performed based on the selection of a pattern with a high resemblance to the target protein using the Swiss Model database.

Results: The results indicate that 6 similar structures were found in the protein database for CBP60g, one of these structures, called the crystal structure of a c6tmiB, had a similarity of 25%. The model chosen for modeling CBP60g protein in Protein Calmodulin-binding protein 60 G AlphaFold DB model of CB60G_ARATH (gene: CBP60G, organism: Arabidopsis thaliana (Mouse-ear cress)) (F4K2R6.1.A) contains 563 amino acids and discovered by AlphaFold v2 with a resolution 3.30 angstroms. The Identity F4K2R6.1.A of pattern with target, protein is 100.

Conclusion: The results of this research can be used in future research and molecular docking and provide basic information to investigate other immune receptors.

Keywords: Receptor, FLS2, 3D structure, 2D structure, Swiss Model Phyre2, Docking

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In silico analysis to investigate gender differential gene expression in gastric cancer (Research Paper)

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Introduction: Gastric cancer (GC) continues to be a significant public health issue and the second-leading cause of cancer-related death, with an estimated one million new cases each year and about 50% of cases occurring in eastern Asia. A taxonomically common phenomenon called sexual dimorphism occurs when males and females in a given species consistently exhibit different traits. Beyond morphological and behavioral characteristics, these variations in humans and other animals also include molecular phenotypes like gene expression. Significant phenotypic gender differences have been linked to sex-specific gene regulation, which may also be a factor in gender differential susceptibility to disease. In this study, we aim to identify the gender differential gene expression in gastric cancer and look into their underlying molecular mechanisms.

Methods: In the current study, one microarray dataset GSE183136 was downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with $|FC| > 0.5$ and P-value < 0.05 were considered to be significant. Functional enrichment analysis was performed on the host genes of DETs (HGTs) and up-stream and down-stream genes of DETS to clarify their possible biological functions.

Results: A total of 135 samples were analyzed in this study, including 44 female and 91 male cases. Using the cut-off criteria, 117 DETs were identified between males and females. Functional enrichment on the HGTs and up and down stream genes of DETs demonstrates 93 down-regulated genes involve in the mevalonate pathway I, Ketone body metabolism, superpathway of geranyl-geranyl diphosphate biosynthesis I and Formation of the ternary complex. Twenty-four up-regulated genes mainly associate with mRNA binding pathway, viral mRNA Translation and Nonsense Mediated Decay.

Conclusion: Our findings provide new insight into the differential risk underlying this cancer as well as molecular distinctions and similarities between genders.

Keywords: Gastric cancer, Microarray analysis

In silico approach for the epitope-based peptide vaccine against the Ebola virus (Research Paper)

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Introduction: Vaccines play an important role in global health by preventing infection and transmission of multiple diseases across the globe. Ebola virus (EBOV) is an enveloped, non-segmented, negative-sense, single-stranded RNA virus of the family Filoviridae that causes severe hemorrhagic fever and is highly lethal. The disease signs and symptoms include anorexia, nausea, vomiting, abdominal and chest pain. Between 2014–2016, West Africa suffered the largest and most complex Ebola outbreak. Considering the importance of producing effective vaccines to prevent the epidemic of this disease, the purpose of this study is to investigate epitope-based peptide vaccine against the Ebola virus by in silico approach.

Methods: In this paper, we choose The Ebola VGP_EBOG4 Envelope glycoprotein. The sequence of this protein in FASTA format was retrieved from the National Center of Biotechnology Information (NCBI). For predicting peptide binding to MHC molecules, IEDB was used. This server is based on the artificial neural network (ANN) approach. This tool measures the binding affinity of a selected sequence to a definite MHC class I or II molecule. Antigenicity and toxicity of the chosen epitopes were then analyzed using vaxijen v2.0 for antigenicity and ToxIBTL for toxicity. One of the important problems with vaccines is their possible allergic reponse in humans. For this matter we analyzed the allergenicity of peptides using AllerTOP v2.0. We can finally choose the best epitope sequence by reviewing binding scores, antigenicity, and allergenicity. In order to show the binding affinity of the selected peptide and HLA, in silico molecular docking was used. Sequences of proposed epitopes that were selected were saved as a PDB file. In the next step, we retrieved receptor HLA-A*0201 (PDB ID: 4U6Y) from RCSB as a PDB file. After optimization and energy minimization, Molecular docking was performed and analyzed using Discovery Studio 3.5 Client software.

Results: We found that the best epitopes, including FFLYDRLAST, AFLILPQAKKDF, and VAFLILPQAKK, can trigger strong immune responses. The binding energy of the best-bound conformation and the ligand RMSD of AFLILPQAKKDF was -185.39 kcal/mol and 59.10 Å respectively. In molecular

docking of this epitope with HLA-A*0201 (PDB ID: 4U6Y), we can see 4 hydrogen bonds by ARG97, ARG65, HIS70, and THR163.

Conclusion: Ebolavirus is one of the most dangerous global epidemics. Therefore, this study is devoted to serving as a platform to hasten vaccine development through the design of an epitope-based peptide vaccine against Ebolavirus using an immunoinformatic approach combined with molecular docking studies. Our study showed the selected epitope has a good affinity toward HLA-A*0201 as a receptor. Both in vivo and in vitro experiments are needed to support these findings.

Keywords: Zaire ebolavirus; vaccine design; immunoinformatic; matrix protein; epitopes

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In Silico Investigation and Discovery of Novel Small Molecule Inhibitors Targeting MET Receptor Tyrosine Kinase in Gastric Cancer (Research Paper)

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Introduction: MET is a receptor tyrosine kinase that transduces signals from the extracellular matrix into the cytoplasm by binding to hepatocyte growth factor/HGF ligand and regulates many physiological processes including proliferation, scattering, morphogenesis and survival. Ligand binding at the cell surface induces autophosphorylation of MET on its intracellular domain that provides docking sites for downstream signaling molecules. Recruitment of downstream effectors by MET leads to the activation of several signaling cascades including the RAS-ERK, PI3 kinase-AKT. While MET-overexpressing tumors are demonstrated to have poorer prognosis, MET pathway seems to be a culprit of cancer invasiveness. Therefore, in this study, we worked on ligand-based design (docking studies) and structure-based design (QSAR and pharmacophore modeling studies) to discover MET receptor tyrosine kinase inhibitors as a therapeutic target in gastric cancer.

Methods: After predicting the first structure of a protein using Expasy and TMHMM portals and predicting the secondary structure of the protein by PRABI PHD, it was defined that the active site locates inside and the protein is unstable considering the instability index>40. Predicting and validating the tertiary structure by PDB/ Uniprot, 4R1V model with the resolution of 1.20 Å was selected for the next steps. Before performing high-throughput screening, tertiary structure of the protein was refined by 3Drefine web server on the basis of evaluating the Ramachandran Plot and its quality factor before and after refinement. Furthermore, we developed a local library of 632 lead-like and purchasable compounds from the Zinc12 Library and prepared them for virtual screening. After performing docking study of ligands by PyRx – Vina Wizard, in the next step, pharmacokinetic (ADME) parameters and drug-likeness of ligand molecules according to Lipinski's rules were predicted by SwissADME. To perform virtual screening of ligands by QSAR analysis, 100 known MET inhibitors from BindingDB with 0.6<IC50<1 were used and prepared for multivariant calibration by Chemoface through PaDEL and then SMLR. After predicting -LogIC50 of selected ligands, PHASE pharmacophore modeling study was done by Schrodinger software.

Results: While 632 compounds were docked, 40 compounds with -10<binding affinity<-8 and RMSD=0 were selected for computational ADME studies through which compounds that inhibited hERG 1/2 were removed and 14 ligands remained for the QSAR study. After building a QSAR model with R2:0.82 and selecting 20% of known inhibitors as the test and 80% as the sample group randomly by the analog mode, -LogIC50 of those 14 ligands were predicted. While -LogIC50 of leads with zinc ID 19796894 and 02739483 were lesser than 0, they were removed and the 00373982 compound had the highest –LogIC50= 1.1. After selecting the OPLS force field, LigPrep was done by Schrodinger to build the model using those 100 MET inhibitors from the BindingDB server. Among developed pharmacophore models, ARR_1 and ARR_2 with Survival Score: 5.014 were selected for screening those 12 filtered Zinc ligands from previous steps. While 10 models were built, the one related to lead with Zinc ID: 13126733 had the highest fitness of 2.143 and then lead with Zinc ID: 19796848 stayed in the second stage with fitness: 1.7.

Conclusion: Throughout this computational drug discovery study, leads with Zinc ID 13126733 and 19796848 were indicated to inhibit MET Receptor Tyrosine Kinase effectively among 632 compounds from Zinc12 Library. Afterward, more evaluations like molecular dynamics simulation studies should be done in the future to further results.

Keywords: MET Receptor Tyrosine Kinase, In Silico Drug Discovery, Gastric Cancer

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In silico screening of inhibitors against human dihydrofolate reductase to identify potential anticancer compounds (Research Paper)

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Introduction: In all species, dihydrofolate reductase (DHFR) is an essential enzyme that regulates the cellular amount of tetrahydrofolate. Human DHFR (hDHFR) activity inhibition results in tetrahydrofolate depletion and cell death. This property has made hDHFR a therapeutic target for cancer. Methotrexate is a wellknown hDHFR inhibitor, but its administration has shown some light to severe adverse effects. Therefore, we aimed to find new potential hDHFR inhibitors using structure-based virtual screening, ADMET prediction, molecular docking, and molecular dynamics simulations. Here, we used the PubChem database to find all compounds with at least 90% structural similarity to known natural DHFR inhibitors. To explore their interaction pattern and estimate their binding affinities, the screened compounds (2023) were subjected to structure-based molecular docking against hDHFR

Methods: Here, compounds having the most remarkable structural resemblance to known natural DHFR inhibitors (Bastadin, Puupehenone, Sanguinarine, and Curcumin) were downloaded from the PubChem database and subjected to structure-based molecular docking against hDHFR. The physicochemical and ADMET characteristics of selected compounds were used to filter them out. Molecular docking was performed to investigate the binding affinity and conformation of the selected compounds in the active site of hDHFR. Finally, MD simulations were applied to assess conformational changes, stability, and the interaction of hDHFR in combination with the chosen compounds compared to MTX. Two compounds were identified as putative hDHFR inhibitors based on the findings.

Results: The fifteen compounds that showed higher binding affinity to the hDHFR than the reference compound (methotrexate) displayed important molecular orientation and interactions with key residues in the enzyme's active site. These compounds were subjected to Lipinski and ADMET prediction. PubChem CIDs: 46886812 and 638190 were identified as putative inhibitors. In addition, molecular dynamics simulations revealed that the binding of compounds (CIDs: 46886812 and 63819) stabilized the hDHFR structure and caused minor conformational changes. Our findings suggest that two compounds (CIDs: 46886812 and 63819) could be promising potential inhibitors of hDHFR in cancer therapy.

Conclusion: In conclusion, the findings of this research demonstrated that two hit compounds (CIDs: 46886812 and 638190) successfully displayed appropriately in silico binding patterns in the active site of hDHFR. Additionally, their acceptable ADMET properties and drug-likeness increase their potential to be developed as anticancer drugs. Finally, MD simulations proved the stability of compounds with hDHFR. Future in vitro and in vivo investigations will be necessary to confirm these two compounds as new hDHFR inhibitors for cancer treatment.

Keywords: Dihydrofolate reductase (DHFR); virtual screening; molecular docking; molecular dynamics simulation;

In-vitro evaluation of cytotoxic, anti-proliferative activity assessment of two tolerogenic probiotics on lung adenocarcinoma (A549 cell line) (Research Paper)

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Introduction: Cancer is a fatal malignancy with high clinical significance and remains one of the major causes of illness and death. The safety and stability of the standard chemotherapeutics drugs and synthetic agents used to manage cancer are affecting the quality of life or contributing for development of drug resistance and are not affordable to the majority of the patients. Therefore, scientists are looking into clinical management of the cancer with high efficiency. Recently the potential impact of the probiotics on the disease has attracted the attention of researchers. Probiotics are useful and nonpathogenic microorganisms in the gastrointestinal tract which can show anticancer activity through the induction of apoptosis. Lactobacilli are a group of probiotics with beneficial effects on prevention of cancer by modulating the proliferation and maintaining homeostasis. Some studies suggest the administration of them efficiently serve as a reservoir in the treatment of a variety of different cancer diseases. The aim of this project was to evaluate the effects of Lactobacillus rhamnosus and Lactobacillus delbrueckii on proliferation of the A549 cell line.

Methods: The studied groups were divided and analyzed as follows (S) only A549 cell line like control group A549 cell line coculture with Lactobacillus rhamnosus A549 cell line coculture with Lactobacillus delbrueckii A549 cell line coculture with both probiotics. The perform analyzes at 48 hours after sowing in 96well plates. Individual groups were subjected to cytotoxicity and cell proliferation tests using MTT assay and within 48 hours. The data were submitted to statistical analysis by ANOVA with a significance level of 5 percent.

Results: This project in under study and the MTT result of the effects of our tolerogenic on A549 cell line will be presented in the congress.

Conclusion: Our results indicated that due to their apoptotic properties and reduction of proliferation on A549 cell line the use of these probiotics could probably represent a new tool for the better management of cancer. Further assessments are required to evaluate our results on the other cancer cell lines in advance to use these probiotics in other extensive trial studies.

Keywords: Lactobacillus, A549, cytotoxicity, tolerogenic probiotics

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Increased Oxysterol Content in Tropical Sea Urchin Echinometra mathaei: From Salinity Stress to Antioxidant Biomarker (Research Paper)

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1.
2.

Introduction: Natural marine compounds have recently developed the focus of amplified exploration attention due to their potential pharmacological functions and minor toxic effects. Cholesterol (cholest-5-en-3β-ol) is the major sterol constituent of animal lipid and fish fat. Oxysterols are oxidation products of cholesterol. Cholestane-3β, 5α, 6β-triol (shortened as triol) is one of the most abundant oxygenated sterols. This triol is derived from cholesterol through autooxidation or in vivo enzymatic procedures and have been recognized in blood, mammalian cells/tissues, and processed foods. Oxysterols indicate vital roles in regulating cholesterol homeostasis, platelet accumulation, apoptosis, and protein prenylation. Recently, oxysterols have been considered as fascinating constituents with miscellaneous biological functions. Furthermore, oxysterols inhibit cell growth, also performs a significant role in the balance among cell division and cell demise.

Methods: Coelomic fluid (up to 2 mL) was withdrawn from animals with a syringe inserted through the peristomial membranes. Extracted coelomic fluid were mixed with a small volume of acetonitrile: methanol (6:4 [v/v]). Oxysterol was deciphered in cell free coelomic fluid from salt stressed and control urchins using high-pressure liquid chromatography-mass spectrometry. For maximal sensitivity and for linearity of the response, the mass spectrometer was activated in multiple-reaction monitoring mode at unit mass resolution. The mass spectrometer was operated in negative electrospray ionization (ESI) mode (even though several analyses worked in positive ion) and the mass spectra collected in the 50–1000 m/z range.

Results: Using LC/MS experiments on coelomic fluid of E. mathaei, one steroid/sterol was identified at m/z 592 as (24R)-Cholesta-5,25-dien-2b,3b,21,24-tetrol 3,21-disulfate with highest content in salt stressed samples. Oxysterols can be ionized readily and lose their hydroxyl/sulphate groups therefore this Oxysterol indicated the major m/z fragment at 369, belonged to cholesterol.

Conclusion: Oxysterols are important cholesterol metabolites involved in cellular membranes permeability and on specific enzyme systems as well as cytotoxic, atherogenic, mutagenic, and carcinogenic actions. Oxysterols have been intensively investigated and many researchers discovered their important natural roles in the human organs/tissues as well as numerous relations to pathological conditions, where diverse oxysterols seem to be promising indicative biomarkers. Oxysterols also have an impact on the physiology of the immune system, from immune cell development and relocation to innate and humoral immune responses. We deciphered higher content of cholesterol and (24R)-Cholesta-5,25-dien-2b,3b,21,24-tetrol 3,21-disulfate at salt stressed urchins. As an unsaturated lipid, cholesterol is susceptible to oxidation in the same manner as polyunsaturated fatty acids and their esters. Therefore oxysterols may be useful markers of oxidative stress or for monitoring of the progression of various disorders and sulfated stroles are the main circulating sterol in plasma which their functions in plasma are not fully defined. Special derivatives of Cholestane were isolated from Sea urchin D. savignyi and sea star.

Keywords: Oxysterols, Cholesterol, Echinometra mathaei, Antioxidant, Stress.

Increasing CRIS-PITCh Method of Gene Editing Efficiency by Using RNP System Delivery (Research Paper)

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Introduction: The main workhorses for producing recombinant therapeutic proteins with complicated glycoforms are Chinese hamster ovary (CHO) cells. Recombinant CHO (rCHO) cell lines are typically created by randomly integrating a gene of interest (GOI) into the genome, then selecting cells that carry the transgene. Lack of control over gene insertion, on the other hand, might result in undesirable phenotypic variability because of the variable accessibility of integration sites for gene expression, also known as position effect variation. These cell lines are hence frequently unstable and gradually exhibit reduced production. To choose the right clones suitable for high and steady expression of recombinant proteins, further screening of several clones is required because of this heterogeneity in expression and genomic composition. Recent releases of the draft genomes of multiple CHO cell lines have made it possible to effectively modify the genomic sequence of CHO cells using engineered nucleases. The CRISPR/Cas9 platform's foundation is a simple base-pairing interaction between an engineered RNA and the targeted genomic site, allowing for quick design, simple use, and low costs. The target locus will normally be repaired by one of the two main DNA damage repair pathways following site-specific DNA double-strand breaks (DSBs) carried on by designed nucleases: the error-prone nonhomologous end-joining (NHEJ) or non-efficient homology-directed repair (HDR) which use long homology arms. An alternative end-joining path called microhomology-mediated end-joining (MMEJ) uses microhomology arms (20–40 bp), which are active during most phases of the cell cycle. Short arms make the donor design simple and economical. In order to use the MMEJ mechanism in CRISPR-mediated knock in, the CRIS-PITCh (Precise Integration into Target

Chromosome) technology has recently been created. The short homology arms of this system's transgene are flanked by sgRNA target sequences, which are used to linearize the donor in vivo and release the transgene. However, the knock-in efficiency of CRIS-PITCH is low. In recent years, attempts have been undertaken to improve CRIS-PITCH's efficiency inside the cell. Plasmid DNA (pDNA), messenger RNA (mRNA), or ribonucleoprotein (RNP, Cas9 protein complexed with sgRNA) are all possible means of delivery for the CRISPR/Cas9 complex. The fastest genome editing is possible thanks to RNP delivery because it does not require intracellular transcription and translation. Transient genome editing, on the other hand, not only enables excellent editing efficiency but also minimizes immunological reactions, insertional mutagenesis, and off-target consequences. The PITCH-CRISPR system in the high-producing cell line CHO-K1 has not been made more effective using this technique. Using this study, we knock-in a landing Pad (LP) with RNP method, the problem of the low efficiency of the PITCH-CRISPR system will be solved to some extent.

Methods: Donor plasmid for the LP construct contained HSV-TK, T2A, and puroR expression units flanked by 30 bp microhomology arms and PITCh gRNA cut sites. For plasmid based transfection an all-in-one plasmid containing tandem U6-PITCh gRNA, U6-genome targeting gRNA, and Cas9 nuclease was used. the single-stranded oligos for PITCh gRNA and Genome-targeting gRNAs synthesized according to Gene Art Precision gRNA Synthesis Kit. Before RNP complex transfection the cells were transfected with the LP donor vector using Lipofectamine 3000 reagent according to the manufacturer's protocols. Two RNP complexes were formed, one containing PITCH gRNA and the other containing genomic target. Transfection with Lipofectamine CRISPRMAX was performed according to manufacturer's protocols. In order to plasmid based assay the cells were cotransfected with the Cas9-sgRNAs vector and LP donor vector using Lipofectamine 3000 reagent. Following puromycin selection, the cell pools were harvested, and genomic DNA was extracted, 5'/3' junction PCR analysis was performed. The intact integration of a transgene was also confirmed with the out-out PCR. The clonal selection was performed using the limiting dilution method. then, PCR analysis was performed on the genomic DNA of each single-cell clone. The relative copy number of integrated thymidine kinase (TK) in single-cell clones was analyzed by quantitative real-time PCR

Results: In this study, by using RNP, we were able to increase the efficiency of the PITCH-CRISPR system in the s100 locus of the CHO-k1 genome by 43% comparing plasmid based CRISPR strategy (22%).

Conclusion: Using this study, we knock-in a landing Pad (LP) with RNP method, so the problem of the low efficiency of the PITCH-CRISPR system will be solved to some extent.

Keywords: CRISPR/Cas9, MMEJ , CRIS-PITCh, sgRNA, CHO cells

Inflammatory status improved following saffron (Crocus sativus L.) and resistance training in elderly hypertensive men (Research Paper)

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Introduction: Currently, there is a great deal of interest in the association between inflammation and hypertension. In older adults, research has demonstrated associations between increased levels of certain inflammatory markers, such as high sensitivity C-reactive protein (hs-CRP), interleukin 6 (IL-6), tumor necrosis factor-α (TNF-α), and hypertension. It is now widely accepted that physical activity helps control blood pressure in patients with hypertension. The physiological functions of the body's immune cells gradually decline with age, leading to impaired skeletal muscle regeneration. Saffron, or Crocus sativus L., is a medicinal herb of the Iridaceae family with anti-inflammatory properties that promote cardioprotective effects. Additionally, saffron has been shown to modulate the levels of some vasoconstrictors and vasodilators in the blood plasma of patients with hypertension. Physical activity is recommended as a significant non-pharmacological solution to attenuate these age-related health conditions. The current study hypothesized that moderate resistance training and saffron consumption might improve inflammation status and reduce high blood pressure in hypertensive older adults, with stronger beneficial effects when the two therapies were combined.

Methods: Elderly hypertensive men were randomly assigned to a control group (C) or one of three experimental groups [saffron consumption (S), resistance training (R), and resistance training + saffron (RS)] for 12 weeks. Inflammatory markers were measured at baseline and following the 12-week intervention period. Patients in S and RS received one tablet containing 200 mg of saffron daily. Primary outcomes were analyzed using univariate analysis of covariance (ANCOVA).

Results: The RS group had significantly greater reductions in, resistin, and IL-6 as compared with the C, S, and R groups (ps < 0.05). There were no differences between groups for TNF-α and hs-CRP (ps > 0.05).

Conclusion: The present study indicates that 12 weeks of resistance training and saffron supplementation, when combined, effectively reduces proinflammatory biomarkers in older hypertensive male patients. We also observed some positive effects for S alone and R alone in increasing HDL

and decreasing, recommended for patients who were unwilling or unable to do one or the other. In general, our findings could lead to future research questions to find out the mechanisms involved in the effects of resistance training or saffron supplementation on how changes in vascular endothelium and its cardiovascular healing consequences and mechanistic changes in some lesser-known inflammatory biomarkers.

Keywords: Hypertensive elderly men, Inflammatory status, Resistance training, Saffron

Insight to anthrax disease and treatment (Review)

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Introduction: Anthrax is a zoonotic disease caused by the Bacillus anthracis bacteria, which is one of the top five important livestock diseases and the second top priority zoonotic disease, next to rabies, in Ethiopia, which remains a major problem for animals and public health in Ethiopia. •Anthrax is a bacterial toxin-mediated zoonotic illness. •It can be contracted by handling, consuming, inhaling, or injecting Bacillus anthracis-contaminated animal by products, such as skins, wool, or meat, or by-product-contaminated objects and fomites. •B. anthracis can be used as a bioweapon. Anthrax is an acute infectious disease of humans and animals, characterized by the appearance of serous and hemorrhagic swellings in the skin and subcutaneous tissues. Anthrax has been a common disease for many centuries and once caused many casualties. Anthrax affects millions of people every year. Abu Ali Ibn Sina, Hippocrates, Homer, Ovid described it as "a disease transmitted from animals to humans." In ancient times, anthrax was called "sacred fire", "Persian fire", "Iranian flame". Three classical clinical forms of the disease, cutaneous, gastrointestinal and inhalation, are seen, all of which can potentially lead to sepsis or meningitis. A new clinical form in drug users has been described recently and named “injectional anthrax” with high mortality (>33%). Inhalation anthrax: This form of disease develops when bacillus spores are directly inhaled during bioterrorism incidents or when contaminated hides are processed in the leather industry. Clinical symptoms include a fever, chills, cough, chest pain, nausea or vomiting, headache, and weariness. Later, the person may also experience shortness of breath and confusion.

Methods: Based on the medical history and physical examination, physicians can choose whether oral or intravenous antibiotics are necessary. Another option for treatment is anthrax antitoxin, which targets anthrax toxins in the body but must be administered in conjunction with antibiotics. Serious instances of anthrax necessitate hospitalization and may call for extensive therapies such as mechanical breathing support, blood pressure support, and excess fluid drainage. The life cycle of Bacillus anthracis in nature. Soil is the main reservoir of the pathogen and is contaminated by spores released from

the carcasses of infected animals. Animals grazing on spore-contaminated land become infected resulting in a new cycle of infection, death and release of spores which can potentially contaminate a new location. Wild carnivores and scavenger birds and flies may also contribute to the spread of spores. Humans can be infected by contact with infected animals or contaminated animal products. The figure was created by Fatma Beyzanur Koyuncu, Medical student in Lokman Hekim University, Ankara).

Results: The majority of clinical forms is cutaneous anthrax. Penicillin G, amoxicillin, ciprofloxacin and doxycycline are widely using in the clinical practice of naturally occurring anthrax. The prevention of human anthrax is based on the control of animal infection, education of animal owners and occupational risk groups. We suggested vaccination of all animals in the afected subcounty and the surrounding areas as well as safe disposal of dead animals. In addition, we suggested that the Ministry of Health and Ministry of Agriculture, Animal Industry, and Fisheries investigate potential anthrax hotspots throughout Uganda, vaccinate animals in areas, where the disease is endemic, and educate the public on the risks of eating meat from animals that died of an unknown cause.

Conclusion: The major cause of anthrax in humans is direct or indirect exposure to infected animal products, whereas the risk factors of anthrax among the animal population are host susceptibility, droughts followed by heavy rains and low levels of pastures hence animals graze close to the ground During this outbreak, case-patients included farmers, butchers, and herdsmen. All were known to have had contact with livestock four days before symptom onset. Contact with livestock included skinning, slaughtering, carrying meat and cleaning the carcasses of the animals. These are mainly male-dominated roles which explains why males are usually the most affected subpopulation during anthrax outbreaks. Tere were no fatalities during this anthrax outbreak. Most case-patients were receiving treatment at the time of the investigation and other exposed persons were given post-exposure prophylaxis

Keywords: anthrax , clinical form , treatment , zoonotic disease , cutaneous anthrax

Insight to cancer treatment (Review)

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Introduction: Cancer treatment is one of the major challenges of modern medicine. Traditional cancer therapies that include chemotherapy, radiation therapy, targeted therapy and immunotherapy, import lots of toxicity problems to patients, because they are not selective to tumor cells. Nanotechnology has been extensively studied and exploited for cancer treatment as nanoparticles can play a significant role as a drug delivery system. Nanoparticle (NP)-based drug delivery systems have shown many advantages in cancer treatment, such as good pharmacokinetics, precise targeting of tumor cells, reduction of side effects, and drug resistance. The NPs used in medical treatment usually have specific sizes, shapes, and surface characteristics as these three aspects have a major influence on the efficiency of the nano-drug delivery and thus control therapeutic efficacy. NPs with a diameter range of 10 to 100 nm are generally considered suitable for cancer therapy, as they can effectively deliver drugs and achieve enhanced permeability and retention (EPR) effect. Smaller particles can easily leak from the normal vasculature (less than 1–2 nm) to damage normal cells and can be easily filtered by kidneys (less than 10 nm in diameter, while particles that are larger than 100 nm are likely to be cleared from circulation by phagocytes.

Methods: Active targeting specifically targets cancer cells through direct interactions between ligands and receptors. The ligands on the surface of NPs are selected to target the molecules that are overexpressed on the surface of cancer cells, which allows them to distinguish targeted cells from healthy cells. The interaction between ligands on NPs and the receptors on the surface of cancer cells induces receptor-mediated endocytosis, which allows internalized NPs to successfully release therapeutic drugs. Therefore, active targeting is particularly suitable for macromolecular drug delivery, such as proteins and siRNAs.

Results: Moreover, the surface characteristics of NPs can influence their bioavailability and half-life. For instance, NPs that are coated with hydrophilic materials such as polyethylene glycol (PEG) lessen the opsonization and therefore avoid clearance by the immune system. Therefore, NPs are generally modified to become hydrophilic, which increases the time period of

drugs in circulation and enhances their penetration and accumulation in tumors.

Conclusion: Targeting of cancer cells specifically is a vital characteristic of nano-carriers for drug delivery, as it enhances the therapeutic efficacy while protecting normal cells from cytotoxicity. The targeting mechanisms can be broadly divided into two categories, passive targeting and active targeting.

Keywords: cancer, nanoparticle, treatment, targeting, active

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Insight to depression during pregnancy (Review)

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Introduction: Pregnancy is a major physiological and psychological life event , but pregnancy does not safeguard women against depressive disorders. rates of depression in women are higher during the childbearing but women with some specific factors like: Genetic _Poor social support _ Unplanned pregnancy and…. Are more vulnerable to depression during pregnancy.

Methods: The biological changes also have a direct effect on mood state concentrations for example: female specific sex steroids would raised during pregnancy and modify parts of the brain involved in mood regulation , also decreasing the dose of serotonin and dopamine which are two important neurotransmitters related to happiness and motivational moods of human would lead to depressive mood and low behavior. But what can we do for this disorder? In this case we are forced to choose a way between bad and worse. But, the main question is treating or not treating? Now we are going to take a look at some negative and positive points of treating this disorder

Results: during pregnancy : unfortunately there are no risk _free decisions for pregnant women with a psychiatric disorder but untreated depression during pregnancy may have negative results such as : 1.risk of miscarriage 2. Baby weight loss after birth and… On the other hand treating this disorder would first lead to clinical participations and this action that is a Interdisciplinary collaboration considered as the first line of treatment but antidepressant medication considered as the second line of treatment which includes many negative affects on fetus like: a significant increase in the risks for major congenital malformations and preterm birth beside this I should add that antidepressant medications are considered as teratogens It is probably due to the role of serotonin in determining the left-right axis.

Conclusion: This review describes best practices for the management of depression in pregnancy, and it provides suggestions for future research.

Keywords: depression-depression during pregnancy-antidepressant-teratogen

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Insight to hemophilia disease and treatment (Review)

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Introduction: Introduction: Nowadays around the world gene therapy is being developed and the most common diseases such as cancer can be treated with gene therapy. According to the U.S. Food and Drug Administration (FDA) ،gene therapy is often referred to as a product that inserts a healthy gene into the patient's body by the appropriate vector to affect the target cells as designed. In the last three decades, hemophilia A and B have been promoted as disorders of gene therapy. Hemophilia A and B are inherited diseases that are dependent on the sex chromosome X that cause clotting disorders. Hemophilia A is caused by mutations in F8C genes that cause deficiency or impairment of factor 8 function. And hemophilia B is caused by mutations in F9 genes that cause deficiency and disorders or factor 9.

Methods: Material methods: Hemorrhage in hemophilia can be undamaged; these bleeds often happen in joints and in muscle tissues. If hemophilia is very severe, with normal activities, bleeding may occur spontaneously, But people with milder hemophilia may occur with trauma. Here's how to treat hemophilia with the help of gene therapy. One of these methods is done with Adeno associated virus. Adeno Associated virus (AAV) is a small virus that has a DNA and because of its good specification ،it is used as vector in gene engineering and gene therapy. One of the advantages of this vector is that it is not pathogenic and protein has a coating that binds the cell and enters the gene into the cell. Gene therapy with AAV simply means that we apply healthy genetic material ،the F9 and F8 genes ،into the vector of the adeno associated virus that we remove viral genes but not end of both sides of DNA , because contains viral information which is necessary for the high level of expression of the healing gene that vector carries, now This vector is injected into the body and targets the liver cells. Another method of treatment hemophilia B is Etranacogene Dezaparvovec.

Results: Results: Tissue factor pathway inhibitor (TFPI) is an endogenous inhibitor of the outer coagulation pathway. Generally, in hemophilia A and B patients, TFPI inhibition is an alternative therapeutic approach that increases the external coagulation pathway.

Conclusion: Conclusion: An experiment has been conducted that assesses the prevalence of anxiety disorders in hemophilia patients who have injected the factor and their families. 100 groups of two hemophilic patients in the age group of 8-15 years who underwent regular coagulation factor injections And their parents were compared to 100 groups of parents whose children were undergo control but not suffering. The prevalence of anxiety was 32% in hemophilia and 16% among the control group. Distress among parents of adolescents with hemophilia was 45% and 24% in control group. Observations indicate that anxiety was higher in older patients and in patients with lower gaps in transmitting coagulation factors As a result ،hemophilia patients and their parents are at higher risk of developing anxiety disorders than others.

Keywords: Hemophilia . Gene therapy . Adeno Associated Virus . Factor . Vector .

Insight to hemophilia, ALL disease and treatment (Review)

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Introduction: Pediatric acute Lymphoblastic leukemia (ALL) is the most common cancer in children and adolescents. Current treatment protocols have very high cure rates. However, the use of chemotherapy agents has increased the incidence of thrombotic events and is the second cause of death in this group of patients. Patients with ALL are susceptible to pulmonary thromboembolic complications (VTE). The pathogenesis and incidence of VTE play an important role and have a significant impact on children. According to the studies, changes in hemostasis of children with leukemia can be detected before treatment. In the studies of Mitchell et al., a significant increase in some coagulation factors, a significant decrease in pre-coagulation hemostatic proteins and natural coagulation inhibitors were observed. It seems that the occurrence of thrombosis in ALL is related to the presence of central venous lines (CVL), comorbidities and the type of treatment performed. Most treatment-related events occur during the induction phase. Asparaginase (ASP) and steroids are the main components of chemotherapy protocols for ALL. It seems that the simultaneous use of steroids increases the risk of thrombotic events. According to the available data, there is a direct relationship between the administration of L-asparaginase and the occurrence of thrombosis. Many related events occur in the venous system; Although arterial thrombosis has also been reported (especially in adults). Thrombosis occurs in half of the cases in the central nervous system (CNS) reported in ALL patients treated with L-asparaginase. The reports of studies by Parasole et al. have shown that patients treated with ASP suffered from ischemic-hemorrhagic strokes.

Methods: Catheter-related thrombosis is the most common thrombotic event in ALL. In the studies of KU et al., it is stated that the use of intravenous catheters along with old age and the presence of concomitant diseases is an important factor for predicting thrombosis in ALL. In the study, it was shown that age plays an important role in the development of thrombotic complications. ; While there is no demonstrable effect on the relationship between gender and the incidence of thrombosis caused by ALL. Treatment of such complications is challenging due to severe thrombocytopenia and high risk of bleeding. Unfractionated heparin (VFH) and low molecular weight

heparin (LMWH) are used in ALL patients to treat acute deep venous thrombosis (DVT) and pulmonary embolism (PE). Vitamin K antagonists are the treatment of choice for VTE, but their use is associated with bleeding in cancer patients.

Results: This study emphasizes the need for prospective studies to identify ALL patients at risk of thrombotic complications. This requires strategies to reduce thrombotic complications, increase safety and The performance of treatment protocols during the course of the disease is reminded.

Conclusion: The results of several clinical trials have shown that replacing heparin with Enoxaparin improved the signs and symptoms of venous thrombosis within a few days and reduced the incidence of bleeding during treatment. However, no improvement in the number of platelets has been observed. The fact that the pathogenesis of coagulation activation in cancer patients is complex and multifactorial is well known. On the other hand, thrombotic events in ALL are one of the important causes of mortality complications. This study emphasizes the need for prospective studies to identify ALL patients at risk of thrombotic complications.

Keywords: Cancer-ALL-IGg-Hemophilia-Thrombosis

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Insight to mRNAs vaccine and effectiveness (Review)

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Introduction: mRNA vaccines take advantage of the mechanism that our cells use to produce protein Our cells produce proteins based on the knowledge contained in our DNA; each gene encodes a unique protein. The genetic information is essential, but cells cannot use it until mRNA molecules convert it into instructions for producing specific proteins. mRNA vaccinations provide ready-to-use mRNA instructions for constructing a specific protein. BNT162b2(Pfizer-Biotech) and mRNA-1273(moderna) both are newly approved mRNA-based COVID-19 vaccines that have shown excellent protection and efficacy.

Methods: Lipid nanoparticle (LNP)-formulated messenger RNA (mRNA) vaccineare a promising platform to prevent infectious diseases as demonstrated by the recent success of SARS-CoV-2 mRNA vaccines. To avoid immune recognition and uncontrolled inflammation, nucleoside-modified mRNA in used. . Our results show that partial substitution of ionizable lipidoid with adjuvant lipidoid not only enhanced mRNA delivery, but also endowed LNPs with Toll-like receptor 7/8agonistic activity, which significantly increased the innate immunity of the SARS-CoV-2 mRNA-LNP vaccine with good tolerability in mice. To verify if adjuvant lipidoid substitution is a generally applicable start – egy to enhance the adaptive immune responses of mRNA-LNP vaccines,we further chose the approved SM-102 LNP formulation for investigation.

Results: Together, all the above results confirm that adjuvant lipidoid substitution can enhance the immunogenicity of clinically relevant SARS-CoV-2 mRNA-LNP vaccines, which holds translational potential.

Conclusion: The results of the above formula demonstrate that C12-TLRa substitution can increase antigen-specific antibody responses and B cell responses of clinically relevant mRNA-LNP vaccines.

Keywords: mRNA-LNP, VACCINES, SARS-COV-2, LIPIDOID, IMMUNE

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Insight to Mucopolysaccharidosis type II (Hunter syndrome) (Review)

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Introduction: Mucopolysaccharidosis type II (MPS II; also known as Hunter syndrome) is a rare lysosomal storage disease. The disease is caused by deficiency of the lysosomal enzyme iduronate-2-sulfatase (I2S), which catalyzes the hydrolysis of 2-sulfate groups on dermatan sulfate and heparan sulfate. Deficiency of I2S enzyme activity in patients with MPS II leads to progressive lysosomal storage of GAGs in the liver, spleen, heart, bones, joints, and respiratory tract. MPS II has two clinical forms: neuronopathic, with CNS involvement, and nonneuronopathic, without involvement of the CNS.

Methods: The disease can be transmitted through the mother, who is the carrier of the mutated gene. The syndrome occurs primarily in male children aged between two and five years, while female children are usually not affected, but a case has been reported in a heterozygous female. Early diagnosis is of great importance for the treatment of Hunter syndrome. Diagnosis of MPS II involves assessment of clinical features, biochemical parameters, and molecular characteristics.

Results: macrocephalic head, coarse facial features, enlarged liver and spleen, lower level of I2S, aortic insufficiency, an enlarged left half of the heart and hearing loss are the symptoms of MPSII.

Conclusion: The current treatments are gene therapy, bone marrow transplantation, Hematopoietic stem cell transplantation, Elaprase which is life-long therapy contains the active substance idursulfase (Enzyme replacement therapy) and Substrate reduction therapy.

Keywords: Mucopolysaccharidosis type II , Hunter syndrome , MPS II , Enzyme replacement therapy , I2S

Insight to multiple sclerossis disease and treatment (Review)

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Introduction: Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system characterized by a highly variable and unpredictable course. demyelinating disease it leads to loss of myelin. loss of myelin it can cause neurological defects such as change of vision, weakness ,behavior difficulties and change of sense. Generally, the first manifestations of MS occur in young patients and predominantly in females before the age of 40 years. The early symptoms of MS are divided into 5 categories: 1- Disorder in movement and walking 2- Disorder in swallow 3- Disorder in Bladder and intestines 4- Sensory disorder 5- Disorder in memory and cognition Of course fatigue and depression are very common conditions diagnosed in people with multiple sclerosis. Fatigue is present in 35–97% of people with MS. It is classified as one of the most serious symptoms interfering with daily activities and influencing the quality of life. Fatigue is defined as a subjective lack of physical and/or mental energy.

Methods: The different disease modifying therapies (DMTs) immunomdulating treaments used of the MS include nterferon beta (IFN-β), glatiramer acetate (GA), natalizumab, fingolimod, mitoxantrone, teriflunomide, dimethyl fumarate, alemtuzumab, daclizumab and ocrelizumab. These drugs are largely available in the USA and Europe. DMTs to reduce the velocity of the disease, to reduce the number of attacks, Reducing the intensity of brain attacks designed but the results of using DMTs are different. whatever drugs be stronger Its complications and risks are more. There are 22 DMTs drugs approved by the FDA for treatment of MS. there are 5 of them on interferon. Which will received through an injection (muscular or subcutaneous . All of these have side effects.

Results: 1-The people who use mitoxantrone they are controlled for heart disease 2- Alemtuzumab as vein is injected It can be dangerous to health. This drug is usually prescribed only when two other drugs have been tried but have not yielded results. 3-Clinical trials about natalizumab showed that patients can Progressive Multifocal Leukoencephalopathy (PML) 4- Fingolimod can cause swelling in the behind of eyes, liver injury and PML. But

this drug is First disease modifying therapies and confirmed by FDA for treatment MS in the children. 5-Teriflunomide is oral treatment and has it side effect as like Headache, hair loss and liver injury.

Conclusion: A definitive cause for MS has not been identified .No definitive cure has been identified for MS but The majority of drugs used for treating MS can cause liver injury and for some of them, the reactivation of hepatitis B virus. It also induces fatigue and depression and it also the secondary fatigue and secondary depression in people with MS may be caused by emotional factors, sleep disorders, pain, the coexistence of other diseases and, the use of some medication.

Keywords: multiple sclerosis (MS) Disorder Disease Liver injury Myelin

Insight to Rota virus disease and treatment (Review)

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Introduction: Rota virus is the leading cause of severe eaten diarrhea worldwide. Despite the global introduction ofvaccinations for rotavirus over a decade ago, rotavirus infections Still Result in >200.00 deaths annually, mastry in low- income countries Rotavirus primavily infects enterocytes and induces diarrhea Through the destruction of absorptive enterocytes. leading to malabsorption intestand section secretion stimulated by rotavirus of the non structural plotein 4 and activation

Methods: nervous system. is associated with substantial hospitalizations and healthcare Rotavirus deaths among children andel causes be large expenditures throughoutAsia enterre Safe and effective Rotavirus vaccines could substantially reduce the A burden at disease. the 15 years since rotavirus vaccine. was introduced the number of laboratory detected rotavirus infectios has been consistently lower them during the prevaccine era. During the cavid-19 Pandemic, rotavirus activity.

Results: was suppressed there may be many rotavirus susceptible. children during the 2021-2022 rotavirus sengan Rotavirus vaccines are 78% effective in preventing hospitalizations.

Conclusion: energy emergency department vistis due to rotavirus diarrhea among children <5 years in the US.

Keywords: Rota viruse, viral, Treatment, diesease,vaccines

insight to the roleof peanutsin microbes and industry (Review)

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Introduction: Peanuts are an energy-rich food that contains significant amounts of fat, protein, carbohydrates, vitamins, minerals, and fat-soluble and water-soluble phytochemicals. Peanuts are consumed worldwide due to their high nutritional value and pleasant or unique taste after roasting or boiling. Lipids, proteins, and carbohydrates not only provide energy, but also provide essential nutrients for normal body functions, such as body fat and muscle mass. Vitamins are required for normal cell function, growth, development, disease prevention, and act as coenzymes during energy production. Due to its high nutrient content, peanuts are used in most developing countries to combat malnutrition. Epidemiological studies have associated the consumption of nuts with a reduction in the incidence of cardiovascular diseases and gallstones in both sexes and diabetes in women. Limited evidence also suggests beneficial effects on high blood pressure, cancer, and inflammation. Also, peanut butter consumption was inversely related to type 2 diabetes. It shows the potential benefits of increased nut and peanut butter consumption in reducing the risk of type 2 diabetes in women. To avoid increasing calorie intake, regular consumption of nuts can be recommended as an alternative to consuming refined grain products or red or processed meat.

Methods: We therefore prospectively examined the association between nut consumption and risk of type 2 diabetes in a large cohort of women from the Nurses' Health Study. Results At baseline in 1980, about 35 percent of women in this group reported almost never eating nuts. 36% consume them less than once a week. 24%, 1 to 4 times a week; and 5 percent, at least 5 times a week. Women who ate more nuts tended to weigh less. Women who ate more nuts smoked less and exercised more. Nut consumption was positively associated with polyunsaturated fats, dietary fiber, magnesium, alcohol and multivitamin supplements. Vegetable and fruit intake was similar for women who frequently ate nuts and those who rarely ate nuts, but women who ate more nuts tended to eat less meat and refined grain products. In a secondary analysis controlling for propensity scores, people who ate nuts at least 5 times per week were still at increased risk of developing diabetes compared to those who never or almost never ate nuts. To further examine

whether the relationship between nut consumption and Whether the risk of type 2 diabetes is independent of other potential risk factors for type 2 diabetes, we performed multivariate analyzes in strata defined by the levels of these factors. We found no obvious changes in relation to these factors, and the inverse association persisted in all subgroups. Peanuts have traditionally been used as a source of oil. However, its annual worldwide harvest of protein has reached nearly 4.5 million tons. India, followed by China and the United States are the major peanut producing states. In recent years, several grain and vegetable based foods that use peanuts as protein supplements have been developed to alleviate the problem of protein calorie malnutrition. Peanuts in the form of flour, protein isolate and flour in the form of a mixture have been determined that the product is very favorable in terms of sensory quality.

Results: Peanut protein lacks some essential amino acids, but its real digestibility is comparable to animal protein, even though different processing methods affect it. Food products occupy an important place in human nutrition for economic and social reasons. Millions of people in Asia and African countries depend on plant products, mainly cereals and vegetables, as their food protein sources.

Conclusion: Among the major oilseed crops, peanuts have special advantages because they can be used in many food forms. With a simple roasting and grinding process, peanuts can be turned into a variety of quality food products. Among the world's peanut eaters, roasting and salting is the most preferred method of eating. Roasted nuts are the most popular among the types of ready-made peanut foods. About 60 percent of the peanuts harvested outside the United States are crushed and used for oil extraction, while 70 percent of the U.S. crop is used for food purposes. In the United States, nearly 52 percent of the domestic food product is peanuts for peanut butter spread, 23 percent for salted peanuts, and 21 percent for confectionery. Peanuts are sold fresh as vegetables, canned, frozen, and roasted. In the crust, roasted and salted, more than 50% are used. Sweets are bakery products and are turned into butter for further use. More than 100 recipes

Keywords: Industerial , Microbes , Peanuts , Aflatoxination

Insilico approaches to identify pathways for infertility associated to endometriosis (Review)

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Introduction: Endometriosis is an estrogen-dependent disease that affects approximately about 10% (190million) of women of reproductive age. The most Common Age-Related endometriosis is 25 to 29 years old and it is observed less in women over 44 years old. Genetic and environmental factors play a role in its occurrence. One of the most common symptoms in advanced level of this disease is infertility. There are several ways to treatment the endometriosis considering as prevention to Infertility such as drug therapy but selecting suitable drug is not easy. Now days, insilico methods have been replaced in vitro and in vivo expriments to predict the best drugs although the target drug must be tested through these experimental methods. The Present insilico study was designed to investigate the genes common between endometriosis and infertility to be the gole of target therapy.

Methods: In this study, we used CTD (The Comparative Toxicogenomics Database) database to identified pathways and genes associated with Endometriosis and infertility. Also we used EnrichNet database to predict the functional association between genes and beside the Gene MANIA website was practiced to generate gene-gene interactions.

Results: Base on the CTD results, we found 162 genes related to endometriosis and 30 genes related to infertility. Five genes were common in both diseases (CYP19A1, ESR2, NR2F2, PAPPA, PRL). Interactions among these genes were shown. Base on string database results, PPI enrichment p-value was 0.00117, that it significantly shown the importance of this network interaction. Among these genes, CYP19A1 and ESR2 were shown better combined Score (0.925) than others. Also through Gene Mania results, these

genes have interaction with each other and with a query list of genes. Also we checked the pathways of these genes and common pathways between endometriosis and infertility.

Conclusion: The five genes are common between endometriosis and infertility that can be as target and candidate for selecting the insilico drug study. In this article, we examine the pathways and metabolisms to answer the following question: Are these pathways can be controlled by designing drugs or natural compounds?

Keywords: Endometriosis-Infertility-Insilico-Pathway

Integration of two practical worlds; Nanotechnology and medicine (Review)

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Introduction: Nanotechnology is known as a rapidly growing and developing technology. The term nanomaterials is used for materials with a size between 1 and 100 nanometers. Medical nanotechnology was first proposed in the late 1950s by Dr. Richard P. Feynman, which has various applications; For example, it is important in the fields of therapeutic indications, preventive signs, diagnostic signs and other related matters. In fact, as medical science progresses, the use of nanoparticles in this science is also increasing. Along with the useful applications of nanoparticles in medical science, their possible toxicity should also be considered. Recent studies have shown that some nanoparticles cause toxicity to humans and thus the environment. In this article, we review the users of nanoparticles in medical science and categorize these different applications.

Methods: To write this article, we used Google Scholar and PubMed databases. We limited the time of the articles between 2019 and 2023 and reviewed the related articles in these 4 years. After categorizing the articles, the articles were used to write different sections. Various words and phrases were used for the search, which included: application of nanoparticles in medical science/application of nanoparticles in drug delivery/application of nanoparticles in medical imaging/application of nanoparticles in veterinary medicine/nanoparticles in head diagnosis/nanoparticles in cancer treatment.

Results: Nanotechnology has a variety of applications in medical science, which we categorize some of these applications below: Veterinary medicine: 1. Management of drugs, vitamins and nutritional supplements 2. Diagnosis and elimination of the causes of infection without using surgery 3. Improvement of growth rate 4. Elimination of reproductive disorders of animals 5. Elimination of digestive problems (for example, elimination of diarrhea in pigs) 6. Production of medical livestock vaccines Medical imaging: Nanoparticles are used for medical imaging due to features such as very small size, suitable half-life in blood circulation, cell absorption and high penetration in the tumor, and suitable targeting power, and help in early diagnosis of the disease. It creates a proper distinction between normal

tissues and abnormal wastes. Forensic Medicine: Some nanoparticles have the ability to detect human fingerprints and in this way help the possibility of discovery at crime scenes. Antimicrobial properties: Some nanoparticles limit the growth of certain microorganisms and also biofilms and destroy them, and in this way they have antimicrobial properties. Other applications of nanoparticles in medicine: orthopedics, dental medicine, genetic engineering and gene therapy, production of biosensors, fluorescent biological tags, tumor destruction through hyperthermia, pharmacotherapy and drug delivery, protection against radiation, making burn ointments, etc.

Conclusion: Although the application of nanoparticles in medical science is still in the research and development stage, it is a progressing knowledge that covers various aspects of medical science. It is expected that in the future, more research will clarify the role and nature of the application of nanoparticles in this science. So that effective processes can be clearly explained. It is also important to note that the knowledge of medical nanotechnology is an interdisciplinary specialty and requires the cooperation of experts in different fields. Another important point is that in addition to the research related to the understanding of the role of nanoparticles in medical science, the research on the possible toxicity of nanoparticles should become more important and the effect of different nanoparticles with different doses on different organs of the human body as well as its impact on the environment should be carefully investigated.

Keywords: Nano technology Nanoparticles medical Medical nanotechnology

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Interference of antihistamine drugs on fertility and drying of vaginal mucosa on non-pregnancy (Review)

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Introduction: A type of herbal suppository that helps a lot to treat rapid menopause and infertility in women, and it is a type of protein that is also useful for vaginal mucosa dryness.

Methods: The materials used in this suppository are: alfalfa, honey, vegetable oils and the main ingredients of the suppository which are examined in the laboratory. We came to this conclusion from the method of sampling and testing on the female cow in the Autotechnican machine, when the female cow was pregnant, the edges of her vagina were dry and bleeding, and there was a possibility of abortion and she might have premature menopause, and despite using From the chemical suppositories, he was still suffering from dryness of the vaginal mucosa, which included the harms caused by it, but with repeated use in a few weeks, we found out that this disease can be completely cured with this herbal suppository.

Results: The obtained results indicate that this suppository is completely herbal and does not have the harmful effects of chemical suppositories, and it treats infertility, and women who suffer from early menopause can overcome this problem by using it, and it is also a type of protein. which treats dryness and vaginal mucus and prevents inflammation of the vagina and genital area

Conclusion: Today, many researches are being conducted in order to achieve a healthy and comprehensive treatment that replaces estrogen, considering that vaginal dryness is one of the most obvious side effects of menopause, and neurological treatments to improve this condition are associated with a large number. . Non-natural methods such as vitamin D suppositories can help significantly in improving dryness, vaginal pallor, and the proliferation of vaginal mucosal epithelium cells, so it is suggested to carry out more comprehensive studies on the characteristics of the effect of vitamin D on the practice. to be Their mode of action may provide for clinical and therapeutic applications in some menopausal women and their use.

Keywords: Vaginal dryness and mucus, infertility, fertility and pregnancy problems, premature menopause,

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INTRODUCE AND COMPARATIVE ANALYSIS STEM CELL THERAPIES IN PARKINSON'S DISEASE (Review)

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Introduction: Parkinson's disease (PD) ranks as the second most prevalent neurodegenerative disorder, following Alzheimer's disease. It can result from genetic mutations and lead to a range of motor and non-motor impairments. The main current treatment is the use of drugs that enhance dopamine in the brain, such as levodopa, by dopamine agonists or inhibition of dopamine degradation. However, in a futuristic approach, cell-based therapies, including regenerating and transplanting dopaminergic neurons into the striatum and other brain regions, hold great promise. These cell therapies draw from various types of stem cells, containing embryonic stem cells (ESCs), hematopoietic stem cells (HSCs), neural stem cells (NSCs), mesenchymal stem cells (MSCs), and induced pluripotent stem cells (iPSCs)

Methods: In this article, we review research related to ESCs, MSCs, and iPSCs based on an extensive search of the PubMed database, along with additional references from the NCBI and OSCI databases. Our focus is on recent research published within the last five years, with a limited number of 2023 review articles serving as references for an overview

Results: Each group promises a bright future for Parkinson's treatment; ESCs are important in preclinical and clinical studies. In examining this group, their unique genes are important in the overexpression of several transcription factors related to dopaminergic mesencephalic phenotype and the improvement of motor symptoms of PD; also, in a dedicated transplant from cryopreserved clinical-grade ESCs, named MSK-DA01, the presence of human Tyrosine hydroxylase cells at the transplant site is confirmed. In a newer way, the use of MSCs has fewer restrictions and is more effective; MSCs can be obtained from both allogeneic and autologous sources. The efficiency of this group of cells is broad, but perhaps the most interesting way of using these cells is the use of extracellular vesicles. These extracellular vesicles or exosomes are the paracrine functional components of MSCs and, as nanoscopic particles, they carry molecules like miRNA. MiRNAs are proven markers of the possible diagnosis and treatment; they also say the gene expression pattern in the stage of the formation of this nucleic acid is effective in the occurrence of the disease. These exosomes help to maintain

the active state of transcription in brain vascular endothelial cells (HBMECs) and have a positive effect on the angiogenesis process; the contents of these exosomes affect angiogenesis by increasing the expression of ICAM1. Angiogenesis is important in the treatment of diseases such as PD because it helps the diffusion of substances along newly formed tissues. On the other hand, advances in the use of iPSCs have a latent potential to serve as a type of cell therapy. All iPSC lines can be differentiated into dopaminergic neurons, providing valuable tools for studying the pathogenesis of PD. It states, that iPSC is a cell therapy product that can be transplanted without the risk of immune rejection and eliminating the need for immunosuppression and related side effects. Therapeutic methods like autologous transplant, allogeneic transplant without matching human leukocyte antigen, and allogeneic transplant with matching are utilized to mitigate the risk of immune rejection. However, a major drawback of autologous grafts is that the transplanted cells may still carry genetic mutations or risk factors contributing to PD. For example, the SNCA gene is responsible for α-synucleinopathies and is a common cause of neurodegeneration. The most prevalent alpha-synucleinopathy arises from the abnormal accumulation of α-syn. Mutations in the PARK2 and GBA genes represent other detrimental mutations.

Conclusion: In conclusion, the purpose of this article is to introduce and compare the performance of three groups: embryonic, mesenchymal, and induced pluripotent stem cells, as cell-based treatments for Parkinson's disease. Most studies conducted reveal similar results in both in vitro and in vivo conditions, with the occurrence of tumorigenesis and teratoma formation being rare. Nonetheless, challenges persist, including identifying suitable transplantation sources, immunogenicity post-transplantation, ethical concerns, and dealing with the limitations of treating advanced diseases. A comprehensive comparison can pave the way for effective treatment. It is noteworthy that mesenchymal stem cells currently represent one of the most debated treatment methods, but is this approach the most efficacious one?

Keywords: Cell therapy, stem cells, Parkinson's disease, dopaminergic neurons, mutation

Investigate function of Wnt/B-Catenin Signaling Pathways in Cancer (Review)

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Introduction: Introduction: Genetic changes are the basic cause of the disease of cancer. The Wnt/-catenin signaling pathway is linked to the control of stem cell pluripotency, self-renewal, and differentiation potential. The Wnt/-catenin pathway is abnormally activated in cancer, which promotes tumor growth, degeneration, and metastasis. A conserved signaling axis involved in a variety of physiological processes, including proliferation, differentiation, apoptosis, migration, invasion, and tissue homeostasis, is the Wnt/-catenin signaling system, also known as the canonical Wnt signaling pathway. There is growing evidence that certain solid tumors and hematological malignancies were able to originate and progress because of disruption of the Wnt/-catenin cascade. This review study aimed to Investigate the function of Wnt/B-Catenin Signaling Pathways in Cancer.

Methods: Search Method: The current study was conducted by scanning scholarly resources such as Google Scholar, Science Direct, Springer, and PubMed for information on investigating the function of Wnt/B-Catenin Signaling Pathways in Cancer

Results: Results: Several co-activators of -catenin-dependent transcription, including CREB binding protein (CBP), are involved in the signaling pathways in various forms of cancer, according to the findings of numerous studies on these pathways. The CBPs are important transcriptional co-activators necessary for numerous cellular functions, as well as being involved in cancer and pathological states in humans. Recent years have seen the development of several CBP inhibitors, some of which have demonstrated positive antineoplastic benefits in preclinical animals with little off-target effects. These inhibitors include PRI-724, ICG001, GNE-781, 1-(1H-indol-1-yl) ethenone, JW67, JW74, NLS-StAx-h, and others. A ground-breaking small molecule antagonist, PRI-724 prevents the interaction between -catenin and CBP. It was promptly hydrolyzed to its active form, C-82, in vivo after being phosphorylated. Preclinical research had demonstrated a significant toxicity profile and PRI-724 elevated sensitization to platinum treatment in chemotherapy-resistant EOC with hyperactivated CBP/-catenin pathway. ICG-001 monotherapy resulted in a decrease in tumor-related features. In an acute

myeloid leukemia (AML) model, GNE-781 demonstrated anti-tumor action. It was also demonstrated that Foxp3 transcript levels decreased in a dose-dependent way. In multiple prostate cancer cell lines, 1-(1H-indol-1-yl) ethenone significantly reduced cell proliferation. JW67 and JW74 were found to specifically inhibit the canonical Wnt pathway at the level of the destruction complex, preventing the development of various intestinal neoplasia animals and colorectal cancer mouse xenograft models

Conclusion: Conclusions: in Conclusions Novel strategies are imperative to improve the outcome of cancer patients. With great advances in the knowledge of molecular basis and the constant effort for improvement, preclinical investigations and clinical trials have been conducted on the Wnt/β-catenin signaling targeted interventions in malignancies. The Wnt/β-catenin signaling targeted regimens have been proven to represent promising candidates for individualized approaches in the treatment of cancer patients. Further investigations are expected to confirm the safety, efficacy, patient stratification and drug delivery of innovative Wnt/β-catenin targeted therapies in cancer.

Keywords: Keywords: Wnt/B-Catenin, Signaling Pathways, Cancer, abnormality, genetic

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Investigate interaction between Ethyl cinnamate and E6 protein (Research Paper)

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Introduction: In this research article, we investigated the interaction between ethyl cinnamate and E6 protein. For this purpose, we used the molecular docking method. E6 produces a protein (also called E6) that simultaneously binds to two host cell proteins called p53 and E6-Associated Protein (E6-AP). the degradation of p53, induced by E6, promotes unregulated cell division, cell growth and cell survival, all characteristics of cancer. according to the numbers, ethyl cinnamate has suitable interaction with E6 protein. So, it could be a drug for treatment of cervical cancer and another types of cancer.

Methods: In this study, we used uniprot website and rcsbpdb website to extract protein's 3D structure as pdb file. After this, we made the protein ready for the project by making changes using Chimera software. E6(4xr8) is the structure which we downloaded and keep the F chain of this Also, by using this software, water molecules were removed from the protein and hydrogen molecules were added to its structure. After this changes, we used pubchem and drugbank to extract 3D Structure of drug as sdf file. molecular docking process was performed by using PyRx software. In this research, the blind docking method was used.

Results: according to the numbers, ethyl cinnamate has suitable interaction with E6 protein. So, it's clear that our compound can be docked to E6 protein the numbers of binding affinity are suitable. also, we have normal range of numbers on RMSD

Conclusion: ethyl cinnamate could be a drug for treatment of cervical cancer and another types of cancer. however, in this article we just worked on in-silico. to prove these conclusions, in-vitro and in-vivo steps should be done.

Keywords: MolecularDocking, Bioinformatic, E6protein, EthylCinnamate, Cancer

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Investigating antibiotic resistance in salmonella strain isolated from meat samples in Yazd (Research Paper)

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Introduction: Salmonella is a gram negative bacteria that is one of the most important food borne pathogens in humans and animals. Infected meat products are the main source of Salmonella, which causes economic losses on poultry, especially young birds, and is important because of its transmissibility from poultry to humans. Salmonellosis is mostly transmitted through the gastrointestinal tract. Therefore, contaminated water and food are a significant source of salmonellosis development.

Methods: In this study, salmonella isolates were isolated from meat samples for 6 months. 6 strains were detected by biochemical tests including XLD, Mac conkey, TSI and Urea. Then an antibiogram test was done for confirmed salmonella isolates.

Results: All isolates were resistant against Erythromycin. 33%, 16.7%, 16.7% were resistant against Trimethoprim/sulfamethoxazole and Ofloxacin and nalidixic acid respectively. All isolated did not show any resistance to sefexim, Cefalotin, Colistin, Amoxicillin, Ciprofloxacin.

Conclusion: Antibiotic resistance has become a dangerous crisis around the world. It seems physicians and veterinarians should prescribe antibiotics in a reasonable way. Also, it is better to omit-the antimicrobial drugs from over-the counter drugs. Especially when this fact is approved that a resistant gene could be transmitted between animals and humans.

Keywords: Salmonella, Resistant, Antibiotics

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Investigating changes in the expression of genes involved in the occurrence of hepatocellular carcinoma: a study Meta-analysis
(Research Paper)

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Introduction: The latest studies show that hepatocellular carcinoma covers about 85% of people with liver cirrhosis; the poor development of hepatocellular carcinoma patients is because the effect of hepatocellular carcinoma in Early stages of the disease is not detectable, early and accurate detection of HCC can significantly improve the clinical treatment effect, with the discovery of HBV vaccine and HCV antiviral therapy, it is promising to reduce the incidence of hepatitis-related HCCs.

Methods: In this study, a set of gene expression data according to the microarray was obtained from the Gene (GEO Expression Omnibus NCBI) database, which is obtained from the accession numbers of the gene for the received data group, including GSE84005 with GPL5175, which is 76 samples. 38 samples Hepatocellular carcinoma cancer tumor and 38 normal hepatocellular carcinoma samples, the data obtained from the downloaded raw Affymetrix CEL file, robust multi-array median RMA for Log2 transformation, normalization and background correction pre-processed for The analysis was carried out through quality meri array in R.

Results: Based on the data that we found from the gene database and according to the analysis that we did in hepatocellular carcinoma, the genes and the path of the genes that increase the expression in different signaling pathways were examined. We have given that it is the same as the previous studies

Conclusion: Based on the analysis and investigations we have done, We concluded that in the tumor tissue relative to the margin, Tumors with -2<

LogFC<2 increased expression and correlated with a P-value < 0.05, It has a meaning.

Keywords: Hepatocellular carcinoma (HCC), long non-coding RNA (lncRNA), mRNA, meta-analysis

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Investigating changes in the microbiota in the stages of gastric cancer progression and its impact on the prevention and treatment of the disease (Review)

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Introduction: Research on the human microbiome has increased in recent years, and researchers have investigated the role of the microbiome in the process of various diseases, including infectious diseases, types of cancer, respiratory diseases, metabolic diseases, and autoimmune diseases. Including gastrointestinal cancers, which in the past caused an important challenge for researchers due to the extremely acidic conditions of the stomach and the limitations of previous culture methods. But today, with the advent of new PCR techniques and metagenomics analyses, the research on stomach microbiota has increased in the last decade.

Methods: By searching the term" intitle: " microbiota " AND gastric cancer AND Helicobacter pylori " in the Google Scholar search engine. Numerous articles were reviewed and screened, and 9 articles were finally carefully investigated.

Results: Currently, the existence of a direct relationship between the diversity of gastric microbiota and cancer progression has not been conclusively proven, but from a mechanistic point of view, the change of microbiota diversity with the progression of gastric cancer is a logical hypothesis. Researchers have shown that sometimes even though the Helicobacter pylori serology test is positive, in more than 90% of patients with acute gastritis caused by Helicobacter and in most patients with advanced gastric cancer AG, IM9, this bacterium is not observed in the stomach tissue; This indicates the disappearance of active Helicobacter pylori infection in the later stages of gastric cancer development. Studies have shown that the primary infection of Helicobacter pylori leads to atrophic gastritis and an increase in the pH level of the stomach, which causes the colonization of new microbes and increases the diversity of species. Compared to people with functional dyspepsia, patients with gastric cancer have high Lactococcus and Lactobacillus genera levels. Bacteria of these two genera in gastric cancer patients with lactic acid secretion can be a source of energy for tumor growth and angiogenesis. In addition, the manipulation of the stomach microbiota, apart from the eradication of Helicobacter pylori, has the potential of a new treatment method

that can also affect the risk of stomach cancer. Research shows that microbes from the Lachnospiracea family are often downregulated in inflammatory processes, so these microbes may regulate inflammation. The Nitrospirae group is present in all patients with gastric cancer but completely absent in patients with chronic gastritis. Several members of the Nitrospirae group are involved in the metabolism of nitrates and nitrites. It has been proven that the consumption of high-salt foods and improper eating habits increase the production of carcinogenic N-nitroso compounds by these bacteria. Propionibacterium acnes, which is a well-known skin flora, is also abundant in gastric tumor tissues, and the production of short-chain fatty acids by it may contribute to the development of lymphocytic gastritis. Reduction of the number of Sphingobium yanoikuyae in patients with gastric cancer compared to patients with It has been shown in research to surface gastritis. This species is able to break down aromatic hydrocarbons that have potential carcinogenic effects. The number of Rhizobiales has increased in patients with intestinal metaplasia compared to patients with chronic superficial gastritis. According to recent data, researchers have found that the genetic transfer of the T4SS secretory pathway between Helicobacter pylori and members of the microbiota, if it occurs, leads to Helicobacter pylori carcinogenesis. Helicobacter pylori, along with other bacteria, can increase stomach cancer. Also, the decrease in gastric acid production along with gastric atrophy following Helicobacter pylori infection may cause the overgrowth of permanent bacteria in addition to the colonization of lower intestinal bacteria. These results suggest that the microbiota may play a role in the development of gastric cancer following Helicobacter pylori infection, but a diverse microbiota may not necessarily be required for the development of gastric cancer.

Conclusion: Gastric cancer increase or decrease the microbiota. As a result, observing certain changes in the microbiota can be used as an alternative to monitoring the progress of the disease.

Keywords: gastric cancer, microbiota, Helicobacter pylori, bacteria

Investigating combinatorial effects of crocin and ionizing radiation on MKN-45 cells (Research Paper)

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Introduction: Crocin, one of the major components in saffron, has been used in traditional medicine for its various health benefits. This carotenoid pigment has therapeutic effects on several human disorders, including cancer, atherosclerosis, hemorrhagic shock, and heart and blood disorders. Gastric cancer is a prevalent form of gastrointestinal malignancies worldwide, with high mortality rate. Resection surgery and use of chemical drugs and ionizing radiation are common therapeutic options for gastric cancer. Nevertheless, survival rate in advance stages is low, mainly due to the metastasis of cancer cells and their chemo and radio resistance. The purpose of current study was to investigate combinatorial effects of crocin and ionizing radiation on gastric cancer cells.

Methods: At first, human gastric cancer cells (MKN-45 cell line) were treated with different concentrations of crocin (2 and 4 mM) for 24 hours. Then after, cells were subjected to varying doses of ionizing radiation (400, 600, and 800 cGy). Following the radiation exposure, cells were allowed to recover for 48 hours and finally alamarBlue reagent was added to cells. After 3 hours incubation, the absorbance was measured in a spectrophotometer at 600 nm.

Results: Finding of the present study showed that combination of crocin and ionizing radiation reduced MKN-45 cell survival. When cells were treated with 2 and 4 mM crocin followed by 400 cGy irradiation, the viability was determined to be 69.1% and 36.6%, respectively. Likewise, after cells were treated with 2 and 4 mM crocin and then exposed to 600 cGy radiation, viability was calculated as 57% and 29.1%, respectively. In addition, upon

treatment with 2 and 4 mM crocin and 800 cGy x-ray dose, the cell viability was reduced down to 30.6% and 22.8%, respectively.

Conclusion: Taken together, our findings indicated that combinatorial use of crocin and ionizing radiation induced toxicity on MKN-45 cells. More research is recommended to assess the effects of our combinatorial approach on other gastric cancer cell lines.

Keywords: Ionizing radiation, Crocin, Combinatorial treatment, Gastric cancer, MKN-45 cells.

Investigating entrepreneurship in nurses (Research Paper)

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Introduction: Entrepreneurship is defined as the process of discovering/co-creating, evaluating, and exploiting opportunities to produce goods and services. Entrepreneurship includes a set of ways adopted in order to ensure the production of capital and better functioning of societies. Entrepreneurship in healthcare is a dynamic and challenging process of creativity and innovation that identifies and exploits previously untapped opportunities. That is, it provides new interventions, products, processes, technologies, and services that address health problems. A nurse entrepreneur is defined as "the owner of a business that provides nursing services of a direct care, educational, research, executive, or consulting nature." Nursing entrepreneurship gives nurses the opportunity to follow their personal views and feelings to improve health outcomes using innovative approaches.

Methods: This study is taken from the Master's thesis, which was conducted with the English keywords Nurse, Entrepreneurship, Entrepreneurial, Nursing, in reliable scientific databases such as PubMed, Google Scholar between 2015 and 2023, and in the initial search 20 articles were found, and after evaluating the title and abstract, 8 articles were selected with the necessary conditions to participate in the present study, and general conclusions were made based on the information in the selected articles.

Results: Nursing profession has content and background knowledge to create entrepreneurial initiatives. The nurse entrepreneur identifies the needs of clients and uses his education, knowledge, and expertise through the creation and development of business in the health care system to effectively respond to these needs. The main stakeholders in nursing entrepreneurship include nurses, clients as clients, nursing profession and society, Each of these four components has roles, responsibilities, and expectations in the

evolution of nursing entrepreneurship. Entrepreneurship for nurses is associated with consequences such as quality care, job and social satisfaction, increased sense of empowerment and independence, time flexibility, maintaining professional identity, self-employment, earning more financial income, and passion for creativity leading to a positive creative environment. Entrepreneurship in nursing facilitates access to health services because it provides different choices closer to the place of residence of the clients.

Conclusion: Although entrepreneurship in nursing is a new focus for the nursing sciences, research in this area is necessary to clarify and identify evidence-based best practices that require the development of nurses' ability to adopt broader health perspectives and challenge more traditional nursing roles. In addition, the knowledge and skills of nurse entrepreneurs can help fill gaps in the healthcare system by increasing the population's access to healthcare services. In the future, more detailed research in this field is needed to expand the scientific foundations of nursing entrepreneurship and its contribution to business performance.

Keywords: Nurse, Nursing, Entrepreneurship, Entrepreneurial

Investigating fungal infections on PSEN1 gene expression in Alzheimer's patients by PCR method review article (Review)

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Introduction: Alzheimer's is a neuropathological disease that causes loss of memory and destruction of cognitive function. Fungal infections can cause changes in the human body at the genetic level and therefore may have an effect on the expression of the PSEN1 gene PCR method can be used to check this effect. One of the factors that may influence the course of Alzheimer's disease is fungal infections. Various fungi can be found in the brains of Alzheimer's patients, and in some cases, fungal infections are more common in the brains of Alzheimer's patients than in healthy people. The PSEN1 gene is a gene related to Alzheimer's disease that plays an important role in the production of amyloid-beta protein Polymerase Chain Reaction (PCR) method has been used to investigate this effect. PCR is a powerful method in biochemistry and molecular biology that is used to amplify and complement DNA sequences using genetic amplification. Using this method, PSEN1 gene expression has been evaluated in Alzheimer's patients with and without fungal infection.

Methods: Collecting brain samples from Alzheimer's patients with fungal infection and Alzheimer's patients without fungal infection, DNA is extracted from the samples. Then primers are designed that join a part of the PSEN1 geneThe PCR solution is prepared, which includes all the necessary materials for the PCR reaction. Then the samples and primers are added to the PCR solution and the PCR reaction is performed in the thermal device. We examine the neuropathological changes in these samples. This method can help investigate the effect of mushrooms on brain function and changes in neural networks in Alzheimer's disease.

Results: The results of this analysis show whether Alzheimer's patients with fungal infection have a difference in PSEN1 gene expression compared to Alzheimer's patients without fungal infection. This method is able to detect and understand the relationship between fungal infections and PSEN1 gene expression in Alzheimer's patients

Conclusion: Early diagnosis and treatment of fungal infections can play an important role in improving the quality of life and management of Alzheimer's patients. Also, a better understanding of the effects of fungal infections in the process of Alzheimer's disease can help to develop new therapeutic and preventive methods in this field. However, it should be noted that other factors such as genetic and environmental factors also play a role in Alzheimer's disease. Therefore, there is a need for further research in this field to improve and confirm the results.

Keywords: Fungal infections,alzheimers disease,PSEN1 gene,pcr,molecular diagnosis, brain tissue sampling.

Investigating impacts of the ABCG2 gene knock out using the high fidelity Crispr-Cas9 in CD44+ triple-negative breast cancer (TNBC) stem cells (Research Paper)

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Introduction: Triple-negative breast cancer (TNBC) is a highly aggressive form of breast cancer characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression. TNBC stem cells, identified by the cell surface marker CD44, have been implicated in tumor initiation, metastasis, and therapy resistance. The ATP-binding cassette sub-family G member 2 (ABCG2) gene, which encodes a drug efflux pump, has been associated with stemness and chemoresistance in various cancer types, including TNBC. In this study, we aimed to investigate the impacts of ABCG2 gene knockout using high-fidelity CRISPR-Cas9 technology in CD44+ TNBC stem cells, utilizing adeno-associated virus (AAV) vectors for efficient gene delivery.

Methods: The study design involved the generation of AAV vectors carrying the CRISPR-Cas9 system targeting the ABCG2 gene. These vectors were then used to transduce CD44+ TNBC stem cells. The efficiency of gene knockout was assessed using various molecular techniques, such as polymerase chain reaction (PCR), Western blotting, and flow cytometry. Additionally, functional assays were performed to evaluate the impact of ABCG2 gene knockout on stemness properties, chemoresistance, and tumorigenic potential of CD44+ TNBC stem cells. AAV vectors are chosen for their numerous advantages in gene therapy applications. These include their non-pathogenic nature, high transduction efficiency, ability to infect both dividing and non-dividing cells, long-term gene expression capability, and low immunogenicity. By utilizing AAV vectors, we aimed to deliver the CRISPR-Cas9 system targeting the ABCG2 gene to CD44+ TNBC stem cells. The ABCG2 gene, also known as the ATP-binding cassette sub-family G member 2, encodes a protein called breast cancer resistance protein (BCRP). This protein is a member of the ATP-binding cassette (ABC) transporter superfamily and is involved in drug efflux, which can contribute to multidrug resistance in cancer cells. While all exons of the ABCG2 gene are important, specific mutations or variants within certain exons can affect the function or expression of the protein. For example, a well-studied genetic variant in the ABCG2 gene is the Q141K polymorphism, which is located in exon 5. This

variant has been associated with altered drug transport activity and drug resistance in certain cancers. In order to achieve this, we can employ the high fidelity Crispr-Cas9 system to specifically target and knockout exon number 5 of the ABCG2 gene in CD44+ TNBC stem cells. We should confirm successful gene editing through genomic DNA sequencing and verified the loss of ABCG2 protein expression using immunoblotting. Subsequently, evaluating the effects of ABCG2 knockout on tumor growth inhibition in CD44+ TNBC stem cells using in vitro and in vivo models is vital. Preliminary results demonstrated that ABCG2 knockout significantly inhibited the growth and proliferation of CD44+ TNBC stem cells compared to control cells. Moreover, ABCG2 knockout does sensitize CD44+ TNBC stem cells to conventional chemotherapeutic agents commonly used in TNBC treatment. Mechanistic investigations reveals that ABCG2 knockout designing appropriate gRNA (via CHOPCHOP) led to increased intracellular drug accumulation and enhanced apoptosis induction in CD44+ TNBC stem cells.

Results: The results of this study will provide valuable insights into the role of ABCG2 in TNBC stem cells and its potential as a therapeutic target. Furthermore, the use of AAV vectors for efficient gene delivery in CD44+ TNBC stem cells will contribute to the advancement of gene therapy strategies for TNBC treatment. Ultimately, this research may lead to the development of novel therapeutic approaches that specifically target TNBC stem cells, improving patient outcomes and reducing the risk of relapse and metastasis. This study contributes to the growing body of knowledge on TNBC stem cell biology and provides a foundation for further research aimed at developing targeted therapies for this challenging disease.

Conclusion: Consequently, the goal of this research is to integrate gene therapy with stem cells which considering that important role in the recurrence on cancer and its formation, by targeting the key gene in drug resistance in them, it can be at the same time, inhibiting drug resistance, metastasis and cancer invasion.

Keywords: TNBC, ABCG2, breast cancer stem cell (CSC), HF-Crispr-Cas9, gene editing

Investigating of impotence of RAS Signaling in Cancer Metastasis (Review)

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Introduction: When cancerous cells separate from the primary tumor, they can travel to other parts of the body through the circulation or lymphatic system. The majority of metastatic malignancies can be controlled but not cured. Treatment can reduce your symptom burden, halt the spread of the cancer, and enhance your quality of life. The RAS family includes some of the earliest oncogenes to be identified, and its identification completely changed how we think about the biology of cancer. The RAS oncogenes, which were first discovered in the 1960s as a viral component that caused the development of sarcomas in rats, were later discovered to be typical elements of the human genome that were capable of converting healthy human cells. This study looked into the ineffectiveness of RAS signaling non-cancer metastasis.

Methods: this review investigating of impotence of ras signaling in cancer metastasis has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: In addition to driving processes essential for the early phases of tumorigenesis, RAS activity is important for the acquisition of more malignant features, including supporting metastasis. In mouse models of colorectal cancer, while primary tumors were characterized by a heterogeneous population of cells bearing both oncogenic KRAS mutations and wild-type KRAS, metastatic sites were largely comprised of more uniform cell populations harbouring oncogenic KRAS. This metastatic phenotype was promoted by transforming growth factor beta (TGF-β) signaling. Distinct from heterogeneity in cellular populations with respect to KRAS mutation status, the acquisition of multiple oncogenic KRAS mutations within single cells through focal amplifications and loss of the wild-type allele (loss of heterozygosity) can promote tumor metastasis and aggressive properties KRAS also supports metastatic dissemination through repression of Raf Kinase Inhibitory Protein (RKIP), a putative tumor suppressor with roles in cell migration, motility, and epithelial-to-mesenchymal transition. Activation of KRAS signaling along with homozygous deletion of LKB1 also known as STK11 or serine/threonine kinase promoted cancer progression and

metastasis in non-small cell lung cancer models. In KRAS-driven pancreatic cancer models, deletion of LKB1 enhanced the tumorigenicity and proliferation rate of cancer cells through enhanced serine biosynthesis and S-adenosyl-methionine (SAM), which supports DNA methylation.

Conclusion: RAS family members are some of the most commonly altered genes in cancer. Perturbations of RAS signaling establish robust oncogenic circuits that drive tumor initiation, progression, growth, and survival. Despite our deep knowledge of the direct downstream signaling effectors of the RAS pathway, continued exploration has revealed new insights into the similarities and differences between RAS family members and their preference for particular cancer types. These efforts have also uncovered the more distal downstream consequences of RAS signaling across cancers, including its rewiring of cellular metabolism and capacity to unlock nutrient scavenging pathways, its role in metastasis, and its dual role in regulating the immune microenvironment. These processes endow cancer cells with the plasticity required for survival in dynamic conditions but also create key vulnerabilities, which can be therapeutically targeted through a number of avenues. Taken together, a deeper understanding of RAS biology will critically inform clinical care and serve as a model for interrogation of other driver alterations in cancer.

Keywords: RAS signalling, Cancer, Metastasis

Investigating pain self-care behaviors in cancer patients referred to the oncology wards of Vali-E-Asr and Mousavi Hospitals of Zanjan, Iran 2021 (Research Paper)

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Introduction: Cancer pain is a distressing symptom for patients and their families that is poorly managed worldwide. Systematic reviews indicate that cancer pain affects approximately 48% of patients with early-stage cancer and increases to between 64 and 75% of patients with advanced disease. Pain is often moderate-to-severe for many patients and can be caused directly by the cancer lesion or by anticancer treatments. Pain negatively impacts patients' quality of life, daily activities, relationships, sleep, appetite, mental health, perception of therapy effectiveness, disease status, quality of services, and even survival. Despite that cancer can be a terminal disease, patients should not be denied the opportunity to live productively and free of pain. Poor pain management places a significant emotional and cost burden on patients, their families, and the healthcare system, with pain being the most common reason for cancer patients to use emergency health services. A wide variety of pain management techniques are available today, which have shifted from simple methods to self-care over time. Considering that the utilization of effective interventions to control pain in cancer patients requires the identification of the existing self-care status, this descriptive cross-sectional study aimed to determine the level of pain self-care behaviors in cancer patients by identifying their existing self-care status.

Methods: This descriptive-cross-sectional study was conducted in 2021 after receiving ethical approval from the Vice-Chancellor for research at Zanjan University of Medical Sciences (Ethics No. IR.ZUMS.REC.1400.290). A total of 152 cancer patients hospitalized in the oncology departments of Vali-E-Asr and Ayatollah Mousavi Hospitals were non-randomly recruited using the convenience sampling method. Data were collected using the Pain Self-Care

Behavior Questionnaire (PSCBQ). The data were first entered into the IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA) and then analyzed using descriptive (Mean, standard deviation, and median) and inferential statistics (Shapiro-Wilk test, and chi-squared test).

Results: The results showed that the self-care behaviors mostly used by the participants consisted of reducing the activity level (79.6%), taking sedatives (75.0%), watching TV (73.0%), napping (72.4%), asking for help (66.4%), and reducing working hours (65.1%). In terms of the effectiveness of self-care behavior in pain relief, the use of sedatives (with a mean score of 6.42 ± 2.31), reducing the activity level (with a mean score of 5.61 ± 2.46), and asking for help (with a mean score of 51.51 ± 2.09) constituted the most effective self-care behavior used for pain relief, respectively.

Conclusion: The findings of the present study indicated that participants' pain self-care was at a low-to-moderate level. The most common self-care behaviors used by participants were reducing activity levels, taking sedatives, watching TV, and napping, the most efficient and effective of which were the consumption of sedatives and reducing the level of activity. Considering the effect of the application of pain self-care behaviors in participants, the design and implementation of patient education programs and the application of effective strategies of pain self-care are necessary. Therefore, it is possible to play an essential role in improving the quality of life of cancer patients by reducing and controlling the complications of their disease.

Keywords: Self-care, Cancer-related pain, cancer, behavior

Investigating radiosensitivity of natural monoterpenoid safranal on MKN-45 cells (Research Paper)

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Introduction: Gastric cancer is a major unmet clinical problem worldwide. The frequency of cases varies greatly across different geographic areas. In our country Iran, for example, the incidence of gastric cancer is around 7300 cases per year, and this malignancy is recognized as the most common cancer in men. Pathogenesis of gastric cancer has been linked to, but not limited, Helicobacter pylori and Epstein Barr virus infection. Surgery, chemotherapy and radiotherapy are common treatments for gastric cancer, however, patients with advance tumor stage have low survival rate. Saffron is one of the oldest spices with various pharmacological effects. In traditional medicine, it has been used to cure vomiting, dental and gingival pain, insomnia, depression, seizures, asthma and bronchitis, to name a few. Saffron is composed of at least four active ingredients including safranal (2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxaldehyde), crocin, crocetin and picrocrocin. As a natural monoterpenoid, safranal has great antioxidant potential and reported to be a good therapeutic agent for diseases arising from oxidative stress. In the present study, we aimed to investigate radiosensitivity of safranal on human gastric cancer cells

Methods: To assess the effects of safranal in combination with ionizing radiation, MKN-45 cells (a human gastric adenocarcinoma cell line) were pretreated with 1.6 mM and 3.2 mM of safranal for 24 h. Then, cells were exposed to 4, 6 and 8 Gy X-ray and after 48 h recovery, cell viability was determined by resazurin assay. Briefly, 10% v/v resazurin solution was added to cells and after 3 h incubation, absorbance was measured at 600 nm.

Results: Obtained results indicated that upon treatment with 1.6 mM safranal followed by 4, 6 and 8 Gy radiation, cell viability was determined as 100%,

99.23% and 89.79% respectively. In addition, after treatment of cells with 3.2 mM safranal followed by 4, 6 and 8 Gy radiation, viability was decreased down to 80.25%, 74.10% and 59.43%, respectively.

Conclusion: Treatment of human gastric cancer cells with the higher concentration of safranal and ionizing radiation reduced viability, however, safranal alone also induced considerable toxic effects on MKN-45 cells. To better evaluate radiosensitizing effects of safranal, more investigation on other gastric cancer cell lines is recommended

Keywords: Radiotherapy, Safranal, Gastric cancer, Natural monoterpenoid

Investigating targeted mutations in tumor Angiogenic factor (VEGF) in colorectal cancer by using edrecolomab antibody engineering
(Research Paper)

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Introduction: VEGF family members, not only in the development but also in the therapy of CRC, in order to fully elucidate their role in carcinogenesis, are extremely important (Dakowicz, Zajkowska et al. 2022). VEGF family (VEGF-A, VEGF-B, VEGF-C, VEGF-D) plays a key role in the processes of blood vessel formation in embryonic development as well as in pathological angiogenesis and lymph angiogenesis, which allow the tumor to grow exponentially (Dabravolski, Khotina et al. 2022). Upon binding their corresponding vascular endothelial growth factor receptors (VEGFRs), VEGFs promote the proliferation and migration of endothelial cells, tube formation, increase vascular permeability and vascular endothelial cell survival, altogether angiogenesis(Bokhari and Hamar 2023) Colorectal cancer is the second leading cause of cancer deaths in men and women worldwide, with an estimated incidence of 1.9 million new cases diagnosed in 2020. The treatment of metastatic colorectal cancer (mCRC) requires multidisciplinary management, and molecular biology knowledge has enabled the incorporation of targeted therapies, such as use of anti-VEGF drugs, into combined chemotherapy regimens(Ortiz-Morales, Toledano-Fonseca et al. 2022) The use of monoclonal antibodies in colorectal and gastric cancers showed the best outcomes when combined with chemotherapy (Bronte, Cicero et al. 2013)even though In this research, high affinity the monoclonal antibody edrecolomab to the VEGF antigen was obtained with the targeted mutations created in the amino acids of the long and small chains of the monoclonal antibody of edraclomab. which is important for angiogenesis signaling, commonly upregulated in mCRC (Hurwitz 2004). Sorting Intolerant from Tolerant (SIFT) is an algorithm that predicts the potential impact of amino acid substitutions on protein function(Sim, Kumar et al. 2012). In this research, we used the Sift software to create targeted mutations, so that by engineering the monoclonal antibody of edercolomab, it can increase its affinity with the VEGF antigen and be useful as a drug candidate in preventing metastatic colorectal cancer.

Methods: Antibody engineering requires the identification of antigen binding domains or variable regions (VR) unique to each antibody(Babrak, McGarvey

et al. 2017) National Center for Biotechnology Information (NCBI) URL (www.ncbi.nlm.nih.gov/gene/), light and heavy chain sequences of the monoclonal antibody edrecolomab were shown. proABC is a web server for predicting CDR regions(Berezin, Glaser et al. 2004) in the antibody binding site that are involved in antigen recognition (http://www.biocomputing.it/proABC). The light and heavy chain sequence was included in this software. Antibody design and amino acid replacement. The amino acids located in the antibody binding site were identified based on the results obtained from proABC web applications. At this stage, the appropriate amino acid was selected for mutation design SIFT analysis was used for prediction (http://sift.jcvi.org/) to determine amino acid substitutions to improve protein function based on the degree of conservation of amino acid residues in sequence alignments derived from closely related sequences(Kumar, Henikoff et al. 2009). Detailed analysis of protein-protein binding was done using HADDOCK software. At http://haddock.science.uu.nl/services/HADDOCK 2.2/. This careful examination was used to determine the interaction and orientation between the two molecules to determine the correct binding between the antigen and the antibodies(De Vries, Van Dijk et al. 2010).

Results: In this study, by creating targeted mutations in the light and heavy chains of the monoclonal antibody of edrecolomab in the 56th amino acid of the heavy chain and the 79th and 105th amino acids of the light chain and using Haddock's software agent, the affinity of the anti-VEGF antigen was compared to the control group of - 85 to -140, and with engineering, we present this variant as the best candidate for treatment of colorectalcancer.

Conclusion: Making specific changes in the genome has been used to analyze gene function and to develop high affinity monoclonal antibody models. Targeted mutations allow the functional examination of specific domains or amino acids in a protein) (Menke 2013). We purposefully created mutations in the amino acid sequence of the light and heavy chains of the edrecolomab antibody. Research has shown that mutations in the amino acids valine and Isoleucine was also found to be largely affected in the mutant, resulting in large decreases in the levels of amino acid-related fatty acids, and these changes seemed to affect the responses in the fluidity of the membrane and cold shock-related phenomena (Choi, Oh et al. 2023) . Amino acids with low molecular weight, such as glycine, alanine, threonine, serine, Proline and cysteine, and the presence of long-chain or branched amino acids, such as tryptophan, and amino acids such as arginine and phenylalanine, despite having a higher molecular weight and replacement with the amino acid lysine. which are necessary to support growth,

development and protein synthesis as well as to reduce stress, can cause high affinity in antibody engineering(Aryal, Dhakal et al. 2022). We created targeted mutations by changing the amino acid valine in the large chain and converting it to isoleucine, changing the amino acid Proline to lysine, and changing the amino acid tryptophan to lysine in the small chain. For antibody development and engineering, antigen-targeting ability and functional characteristics, including antigen-binding affinity, target specificity, biological efficacy through epitope analysis, and develop ability characteristics by creating targeted mutations are considered(Kim, McFee et al. 2023) In this study, targeted mutations in the tumor angiogenic factor(VGEF) in colorectal cancer using the engineering of the Edrecolomab antibody caused high affinity.

Keywords: monoclonal antibody engineering , Tumor angiogenic factor, affinity , Antigen

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Investigating the antimicrobial effects and mechanism of action of antimicrobial peptides derived from the skin and brain of Bombina maxima (Review)

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Introduction: Nowadays, due to the development of drug resistance in microorganisms, the need for a drug alternative is felt. Antimicrobial peptides (AMPs) are a class of active oligopeptides that are toxic to pathogens. AMPs are widely distributed in nature, and examples have been reported from microorganisms, plants, invertebrates, fish, amphibians, birds, and mammals. Amphibians are widely distributed in different continents except for polar regions. They are important sources for the isolation, purification, and identification of natural compounds including peptides with different functions. AMPs play an important role in repelling invading pathogens. Their other biological functions are endotoxin neutralization, chemotaxis, anti-inflammatory and wound healing. A large number of peptides have been isolated from Bombina maxima skin and brain secretions. Peptides belonging to the maximin family have strong antimicrobial activity and are very exciting candidates for drug development. In this research, we focus on Maximin 1,3 H5, which has received more attention than others.

Methods: An online search of published medical articles through PubMed, Scopus, Web of Science, and Google Scholar using the terms "Bombina maxima", "AMP", " Maximin H5", "maximin1", and "Maximin3". Numerous articles were reviewed and screened, and 19 articles were finally carefully investigated.

Results: AMPs are natural antibiotics known for their broad-spectrum resistance against bacteria, fungi, viruses, and parasites and for influencing host immune responses. In addition to antimicrobial activity, some antimicrobial peptides have biological activities such as anti-tumor and anti-HIV. Different from the bactericidal principle of traditional antibiotics with a single target, AMPs due to their broad-spectrum antibacterial properties can destroy pathogens by damaging multiple targets, which can greatly reduce the emergence of drug-resistant bacteria, and makes them one of the best

alternatives for comprehensive antibiotics. The following table is an overview of some known maxims. maximins, a family of linear cationic peptides from skin secretions of B. maxima, differ from previously reported BLPs from different Bombina species in both structure and potency of biological activity. Due to their wide and distinct spectrum of biological activity (antimicrobial, antitumor, anti-HIV, spermicidal, potential new targets in mammals) on membranes, the central nervous system, and the gastrointestinal tract, they seem to have interesting potential for therapeutic application. Information about anionic peptides isolated from anuran amphibians, which could be part of the innate defense system, is scarce. maximin H5 is an example of this category, metal ions did not affect its antimicrobial power, this peptide creates a hemolytic effect by forming a diagonally oriented α-helix structure and inserting a tilted membrane. Maximin S1 has 14 amino acids and S2-S5 has 18 amino acids. Maximin 1-8, 10, 11)Except for 6-8 which have 20 amino acids, the rest have 27 amino acids(and Maximin H1, 3-5, 7, 9, 10, 12, 15, 16)Most of them have 20 amino acids(are other examples of antimicrobial peptides from Bombina maxima skin. Maximin 1 with the sequence: Gly-Ile-Gly-Thr-Lys-Ile-Leu-Gly-Gly-Val-Lys-Thr-Ala-Leu-Lys-Gly-Ala-Leu-Lys-Glu-Leu-Ala-Ser-Thr-Tyr-Ala-Asn 27 amino acids long, is a cationic and amphipathic antimicrobial peptide found in Bombina skin and brain secretions. Maximin1 is biologically interesting, as it possesses little hemolytic activity, and exhibits potent antimicrobial, anticancer, antiviral, anticancer, and spermicidal activity. This peptide is amphipathic and there is a clear separation between its polar and non-polar amino acids. Only a few amino acid differences distinguish maximin 3 from maximin 1 (position 4: tyrosine to glycine, position 8: glycine to serine, position 10: valine to leucine, position 18: leucine to alanine, position 26: alanine to leucine) that the change made in position 8 seems important. The first 22 amino acids form an alpha helix. Flexibility is observed around glycines 9 and 16 in the direction of hemolytic activity. This peptide has received much attention due to its anti-HIV properties.

Conclusion: Recombined and genetically engineered maxi mins are the best alternative or companion to traditional antibiotics due to their specific characteristics and are a promising way to prevent tumors and HIV viruses, etc. Researchers are investigating existing problems such as high synthesis cost, low efficacy, toxicity, etc. The present study investigates the maximins obtained from the skin and brain secretions of Bombina maxima.

Keywords: AMP Bombina maxima Maximin H5 maximin1 Maximin3

Investigating the compounds of burdock root and nettle leaves in inhibiting ESBL enzyme in urinary tract infection (Research Paper)

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Introduction: Urinary tract infections are among the most common infectious diseases worldwide, causing approximately 150 million cases each year, but they remain understudied (Murray BO et al.,2021). Urinary tract infection (UTI) is an inflammatory condition caused by the presence and growth of microorganisms anywhere in the urinary tract. This may be a lower urinary tract infection (urethritis, cystitis) and/or an upper urinary tract infection (Johnson B et al.,2021). Urinary tract infections place an immediate burden on the patient, including physical and emotional distress, as well as the risk of bacteremia and sepsis. For many patients, discomfort and the risk of urinary tract infections become recurring problems. About 1 in 4 young patients will have recurrent UTIs within 6 months of the first episode, and the risk of recurrence is greatly increased in those who have had multiple episodes(Langford BJ et al.,2021). 2-Hydroxybenzoic or salicylic acid (SA), recognized in 1992 as the sixth plant hormone, belongs to the family of natural phenolic compounds having an aromatic benzene ring with one or more hydroxyl groups (Bagautdinova ZZ et al.,2022). Among species, salicylic acid (SA) is widely distributed throughout the plant kingdom. The basic level of SA is different. It usually exists as a free fraction or as glycosylated, methylated compounds, glucose esters or amino acids) Janda T et al.,2020). It is a polyhydroxyflavonol compound consisting of pale yellow crystals and is easily soluble in methanol, acetonitrile, ethanol and other polar solvents (Song X et al.,2021). The structure of myristin is related to the structures of many other phenolic compounds such as quercetin, murine, kaempferol and fistin. Due to structural similarities, myristin is also known as hydroxyquercetin (Imran M et al.,2021). Quercetin, a name derived from quercetum (oak forest), has been in use since 1857. The name occurs widely in natural plants, including apples, berries, Brassica vegetables, capers , grapes, onions, green onions, tea and tomatoes. as well as in many seeds, nuts, flowers, bark and leaves (Yang D et al.,2020). Salicin is one of the natural compounds extracted from plants. Salicin is the precursor to the synthesis of salicylic acid and aspirin with undeniable anti-inflammatory effects(Saracila M et al.,2023). Rutin, also known as rutoside, rutinum, vitamin P, quercetin-3-O-rutinoside

and sophorin, is found in many plants such as tea, buckwheat, tobacco and citrus fruits(Siti HN et al.,2020). Isoramantine is a plant-derived secondary metabolite that belongs to the family of flavonoids and specifically to the group of flavonols. Flavonoids are a large group of bioactive phytochemicals consisting of two phenolic benzene rings and one heterocyclic ring) González-Arceo M et al.,2022). Flavonols are the most common flavonoid chemical structure and are present in approximately two-thirds of the diets of Western societies. They are responsible for the color and flavor of food, prevent the oxidation of fats, and protect vitamins and enzymes. Examples of these flavonoids are kaempferol, quercetin, myristicin and isoramantin) Silva dos Santos J et al.,2021).

Methods: In this research, the Hdock server was used to perform molecular docking. For this purpose, the ligand and protein files were uploaded on the website and the result of docking was observed. In this research, compounds with medicinal properties were investigated. The structures of the desired compounds were obtained from http://pubchem.ncbi.nlm.nih.gov. Names and structural details of studied compounds are given in Table 1. The appropriate crystal structure of the enzyme containing the central catalytic part was selected and downloaded from http://www.rcsb.org/pdb. Enzyme code on this site is 2zmx with 1/33 angstrom resolution.Preparation of ligand and protein tyrosinase for docking: The two-dimensional structure of the desired ligands was drawn by the Hyperchem program and then optimized in terms of energy by the same software. In the next step, the extra structures of the enzyme, including water and non-protein parts, were removed using Discovery software, and after that, it was fully optimized and prepared for molecular docking by Chimera program. The studied protein file and ligand file were uploaded and submitted in the HDock server. In the next step, the top 10 molecular docking models were downloaded and the model with the most negative binding energy was fully investigated.Observation and analysis of docking results: after performing the docking operation, the results include Most favored regions and Disallowed regions, binding energy of ligands, types of ligand interactions with protein including hydrogen interactions, hydrophobic interactions, types of pi number interactions, interactions with ions Copper in the active site of the enzyme and other things can be seen and analyzed. In order to obtain the mentioned information, Discovery software and two Pdb Sum Generate, HDock servers were used.

Results: In inhibiting the Esbl enzyme, the energy level of the compounds that have formed hydrogen bonds in the active site of the enzyme are as follows: salicylic acid-94/42, myristicin-172/70, kaempferol-167/89, quercetin-175/58, salicin-29 149/149, rutin-77/93, luteonin-54/165, visuramentin-185.

Conclusion: Flavonols are the most common flavonoid chemical structure and are present in approximately two-thirds of the diets of Western societies. They are responsible for the color and flavor of food, prevent the oxidation of fats, and protect vitamins and enzymes. Examples of these flavonoids are kaempferol, quercetin, myristicin and isoramantin. . In a study conducted by Kullappan Malathi et al. in 2018 on bioinformatics methods to discover new drugs and compounds OxA_10 ESBL and imipenem establish hydrogen bonds with phe208, ser67, Glu244 and Arg250 in the active site of the enzyme.Additionally, in a study conducted by Mahmoud A et al. in 2020, for the isolation and bioassay-guided linkage of potential beta-lactamase inhibitors from Clutia myricoides, their 1, 2 and 3 combinations with thr235, ser237, ser70, Asn104 and Asn132 in the active site of the enzyme was established as a hydrogen bond. while salicylic acid, myristin, kaempferol, quercetin, isoramentin, luteonin with ser70 and Asn132, and salicin with ser237 and rutin with ser70 in the active site of the enzyme established hydrogen bonds.

Keywords: Urinary tract infection, effective compounds, binding energy, molecular docking, Esbl

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Investigating the correlation between women's personality type and spousal abuse (Review)

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Introduction: Violence against women is an important public health problem that has short-term and long-term mental and physical health consequences for women and their families (1). Factors that contribute to the occurrence of domestic violence may include the personality characteristics of couples and the ways in which couples manage each other's emotions (2). The present study was conducted with the aim of determining the correlation between women's personality types and spousal abuse.

Methods: The present study is a comprehensive review study. In this study, 426 articles were obtained through electronic search by entering the desired keywords in Pubmed, Science Direct, Cochrane Library, SID, Magiran and Irandoc databases from the time period covered by these banks until 2023. Finally, 4 studies (2 cross-sectional, 2 descriptive-analytical) in the period from 2002 to 2023, which investigated the correlation between personality traits in women and partner violence, were analyzed.

Results: A review of the available articles showed that some personality traits of women are related to spousal abuse. According to the results of a study, agreeableness, conscientiousness and extroversion have a negative correlation with domestic violence. (3). Another study found a significant relationship between neuroticism, extroversion, agreeableness and conscientiousness with violence. So that neurotic women were more abused by their husbands ($p<0.0001$) and women who were extroverted, agreeable and conscientious were less abused by their husbands (4). In a study of neuroticism, psychological violence and physicality, conscientiousness predicted sexual violence and extroversion predicted physical violence ($p\leq0.05$) (5). In another study, there was a positive correlation between neurotic personality ($r=0.318$, $p<0.001$) with domestic violence and negative correlation between extroversion personality (-0.280, $r=P<0.001$), agreeableness (-0.201, $r=P<0.002$) and conscientiousness with domestic violence (265/265) -0, $r=0.001$ <P) there is (6).

Conclusion: Some personality traits such as neuroticism and extroversion are more related to domestic violence. Therefore, by identifying personality traits, it is possible to provide more appropriate treatment outcomes for mental health professionals and effectively prevent the increase of domestic violence.

Keywords: spousal abuse; Domestic violence; Personality traits, personality types

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Investigating the cytotoxicity of of Actinomycete bacteria extract on adipose mesenchymal stem cells of Wistar rat (Research Paper)

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Introduction: Aim and background: Actinomycete (Ac) bacteria contain several bioactive metabolites with anti-bacterial, anti-cancer, and anti-inflammatory effects. Their cultivation and laboratory development are easy, which makes them a suitable source for the extraction of medicinal metabolites. Adipose tissue mesenchymal stem cells (AMSCs) are multipotent stem cells with capacity to regenerate tissue damages; they also has applied in inflammatory diseases due to immunomodulatory potential. So, evaluating the effect of new metabolites or medications on them is an essential issue. In the current study the effect of an Iranian endemic Ac extract was investigated on rat AMSCs.

Methods: Materials and Method Ac was collected from Garmsar region of Iran and cultivated in 25 plates in the basic culture medium by grass method. Extraction was done with ethyl acetate solvent. AMSCs were isolated from male Wistar rats and were characterized by flow cytometry. GC-Mass was performed to determine metabolites of Ac extract. Ac extract was dissolved in dimethyl sulfoxide and 5-100 µg/ml concentrations were applied on AMSCs for 48 hours. The level of cytotoxicity was determined by MTT assay.

Results: Results: Flow cytometry results confirmed the mesenchymal characteristic of the cells. GS-Mass showed higher anti-oxidant content of Ac extract. Ac extract had a protective effect on ASC viability at 5 - 25 µg/ml but at concentration more than 25 µg/ml, it caused toxicity on AMSCs. The IC50 (Median Inhibition Concentration) of Ac extract was measured as 64.12 µg/ml.

Conclusion: Conclusion: This study proved that our new Ac extract contains secondary metabolites and can be considered for the production of biological compounds.

Keywords: Keywords: Actinomycetes, Metabolite, Mesenchymal stem cells, Cell Viability

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Investigating the Diagnostic Accuracy of Focused Assessment with Sonography in Trauma (FAST) Compared to CT Scan in Patients with Blunt Abdominal Trauma (Research Paper)

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Introduction: Objective: Focused assessment with sonography in trauma (FAST) is a very valuable part of the initial examination in emergency care. The aim of this study was to investigate the diagnostic power of FAST ultrasound in diagnosing intra-abdominal visceral injuries caused by trauma.

Methods: Method: A retrospective cross-sectional descriptive study on 150 patients who visited the emergency department of Khatam Shahr Zahedan Hospital in the southeast of Iran during 2021 and were admitted to the study with the diagnosis of blunt abdominal trauma. The results of FAST ultrasound were compared with CT results. The sensitivity, specificity, positive and negative predictive value of FAST compared to CT as a standard were measured.

Results: Findings: The patients included 109 men and 41 women with an average age of 35.7 ± 25.8 years, the youngest was 19 years old and the oldest was 70 years old. The most injuries were due to accidents (40 cases), falls (50 cases) and impact (60 cases). The condition of the patients was such that about 97% of the patients had triage level 2. The sensitivity was 75%, the specificity was 98.6%, the positive predictive value was 60%, and the negative predictive value was 99.3%.

Conclusion: Conclusion: Ultrasound is a reliable tool for examining trauma patients and due to the constant presence of emergency medicine specialists at the patient's bedside in the early moments, it plays a significant role in improving the treatment protocol of trauma patients.

Keywords: Keywords: blunt abdominal trauma, FAST ultrasound, CT, sensitivity, specificity.

Investigating the effect of aqueous extracts of C. sativum, T. polium, Mentha and Z. officinale plants on oral microorganisms in a laboratory environment (Review)

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1. Allameh Helli Malard

Introduction: A large number of medicinal plants are used all over the world as natural resources to treat diseases and maintain human health. These plants have strong medicinal and antibacterial properties due to the natural active compounds in them. One of the common methods of using medicinal plants is extracting water that contains the active compounds found in the plant. In the human mouth, there are microorganisms such as bacteria and fungi that can cause oral diseases such as gingivitis, tooth decay and bad breath. To control these microorganisms and prevent oral diseases, it is very important to use antibacterials and antifungals. In this research, the effect of aqueous extracts of Coriandrum sativum, Teucrium polium, Mentha and Zingiber officinale plants on oral microorganisms has been investigated in a laboratory environment. Using aqueous extraction, the active compounds in these plants are evaluated as antibacterial and antifungal in a laboratory environment. The results of this research can help to better understand the antibacterial and antifungal effects of aqueous extracts of C. sativum, T. polium, Mentha and Z. officinale on oral microorganisms and be a new treatment method to control diseases and maintain oral health.

Methods: Preparation of aqueous extract: in the first step, C. Sativum, T. polium, Mentha and Z. officinale plants were prepared and then the aqueous extract of these plants was prepared. Then, the obtained aqueous extracts were concentrated in a water bath device and in the last step, the obtained extracts were sterilized by UV rays. Cultivation of microorganisms: After preparing the semi-solid culture medium, under the microbial hood, oral microorganisms were removed from the mouth of the target person by means of a swab and cultured on 24 of the semi-solid culture mediums. No additives were added to 2 of the semi-solid culture media and they remained devoid of microorganisms to be considered as zero group. Then the culture mediums were placed in an incubator at 37°C for two days and nights. Determining the antibacterial effect of the extracts: In order to determine the antibacterial effect of the aqueous extract of the desired plants, treatment was done on the microbial population of oral microorganisms, for this purpose, five treatments were formed: First treatment: zero group (culture medium without microorganisms and without any additives) Second treatment: control group

(oral microorganism culture medium without any additives) The third treatment: extract treatment (aqueous extract of the desired plants in the cultivation environment) Fourth treatment: ampicillin treatment (ampicillin antibiotic in culture medium) The fifth treatment: Penicillin treatment (penicillin g benzathine antibiotic in culture medium) The treatments were evaluated in 24 and 48 hours. In order to minimize the test error, 3 samples were prepared from the second to fifth treatments and 2 samples from the first treatment. The information collected in the experimental design was evaluated in terms of significance.

Results: After keeping the cultures in the incubator for two days, they were examined. Ampicillin antibiotic and C. sativum aqueous extract had more inhibitory properties than other substances. It can be said that the antibiotic ampicillin has almost completely prevented the growth of microorganisms. The aqueous extract of Z. officinale, aqueous extract of Mentha, aqueous extract of T. polium, the combination of the extracts of the four plants, and penicillin G benzathine antibiotic had very little inhibition. Zero group was left without growth of microorganism.

Conclusion: Ampicillin showed the highest inhibitory effect and C. sativum aqueous extract had a slightly lower inhibitory effect, but Mentha aqueous extract, Z. officinale aqueous extract, T. polium aqueous extract, the combination of the extracts of the 4 plants and penicillin G benzathine antibiotic had very little inhibitory effect. It is recommended to use C. sativum extract or its active ingredients in mouthwash and toothpaste. But the use of ampicillin antibiotic can cause problems. Coriander extract is antifungal, antibacterial and a herbal antibiotic and can be used to treat infections and prevent tooth decay.

Keywords: Oral microorganisms, C. sativum, T. polium, Mentha, Z. officinale.

Investigating the effect of cognitive behavioral therapy on mental disorders in elderly men with prostate cancer: a systematic review (Review)

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Introduction: Prostate cancer is the most common male cancer that affects various aspects of personal health, including mental health. Prostate cancer has a negative effect on the quality of life, and stress and anxiety aggravate this negative effect. Given that the elderly with cancer suffer from mental disorders, the present study aims to determine the effect of cognitive behavioral therapy on mental disorders in elderly men with cancer. It was done for prostate cancer.

Methods: This systematic review was conducted by searching SID, Pubmed, Magiran, GoogleCochrane, Scholar and Scopus databases and search engines. Articles were searched with the keywords of cognitive behavioral therapy, mental disorders, elderly, mental health, life expectancy, quality of life, depression, anxiety, stress, prostate cancer and their English equivalent without considering the time limit. The exclusion criteria of articles included studies about other cancers.

Results: After evaluating the quality of the articles, among the 87 articles, 21 related articles were included in the study. The results of various studies showed that cognitive behavioral therapy increased self-efficacy and quality of life, life expectancy, improved mental health and hope, and significantly improved the sleep quality of elderly men with prostate cancer and significantly reduced the symptoms of depression, stress and anxiety in This men reduced.

Conclusion: Anxiety and depression reduce the quality of life of patients with prostate cancer. Along with medical treatments, it seems that the implementation of appropriate psychological interventions is effective in order

to increase the quality of life of patients with prostate cancer. Cognitive behavioral therapy has a positive effect on various aspects of men's mental health. The elderly have prostate cancer, so this method in oncology centers can be considered as a complementary treatment along with medical treatments for these elderly.

Keywords: Cognitive behavioral therapy, mental disorders, elderly, depression, anxiety, stress, prostate cance

Investigating the effect of common mutation of SLC3A1,CLDN14,ALPLgenes in kidney stone patients in Tehran (Review)

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Introduction: Kidney stone disease, also known as nephrolithiasis or urolithiasis, is one of the oldest diseases known to medicine. It is estimated that 1-15% individuals suffer from kidney stone formation at some point during their lifetime, and the prevalence and incidence of kidney stone is reported to be increasing worldwide .Without proper treatment, kidney stones can cause the blockage of the ureter, blood in the urine, frequent urinary tract infections, vomiting or painful urination, culminating in the permanent functional damage of the kidneys .The worldwide prevalence of urolithiasis has increased over the past decades. Urolithiasis is often a recurrent and lifelong disease with a recurrence rate of 50% within 5-10 years and 75% within 20 years . Some studies have indicated that an increase in kidney stone occurrence is expected, due to multiple environmental factors, including changes in lifestyle and dietary habits, as well as global warming . Due to its high prevalence in adults of working age, kidney stone disease has a substantial impact on the individual and society, and has become a public health issue, particularly in populations residing in regions with a hot and dry climate . There are mainly five types of kidney stones according to the mineralogical composition, including calcium oxalate (CaOx; 65.9%), carbapatite (15.6%), urate (12.4%), struvite [(magnesium ammonium phosphate), 2.7%], brushite (1.7%) . Kidney stones can be broadly categorized into calcareous (calcium containing) stones and non-calcareous stones. The most common types of human kidney stones are CaOx and calcium phosphate , either alone or combined, which are calcareous and radio-opaque stones . Kidney stones form at a foundation of CaP termed Randall's plaques , which begins at the basement membranes of thin limbs of the loop of Henle on the renal papillary surface . CaOx and

urate stones exhibit a higher occurrence in males, whereas higher percentages of carbapatite and struvite stones are observed in females than in males . Several GWAS have been performed in kidney stone. In a GWAS, several million common DNA variants, so-called single nucleotide polymorphisms (SNPs) scattered throughout the genome, are tested in large groups for association with a trait. Our aim is to investigate the SNP in the common genes SLC3A1, CLDN14, ALPL, which causes early diagnosis in people with kidney stone disease and helps to improve these people in the society. Our subject by evaluating the occurrence of common mutations with the examined SNPs(Rs200483989,Rs219780,RS1256328)

Methods: Using the PCR technique, The primary purpose of polymerase chain reaction (PCR) is to rapidly make many copies of a specific region of DNA or RNA so that it can be adequately identified, often by agarose gel electrophoresis. PCR is commonly used to amplify, modify and clone genes for expression studies. There are many uses for PCR, including paternity testing, biological relationships, mouse genotyping, diagnosing genetic diseases, forensics, and finding bacteria and viruses. we check the SNP sequences of SLC3A1,CLDN14and ALPL genes ،Single nucleotide polymorphisms (SNPs) are DNA sequence changes that occur when a single nucleotide in the genome is different in paired chromosomes. Some SNPs change the amino acid sequence of a protein in the coding region, and others in the coding region. , do not affect the protein sequence. SNPs outside the coding region may also affect transcription factor binding, gene splicing, or mRNA degradation. With or without such effects on the biological function of gene products, SNPs serve as markers for investigating imbalances. Linkage and detection of genetic polymorphisms are very useful in population genetics research and medical sciencewith gene expression , and by observing the electrophoresis gel, we find out the effect of gene expression and mutation of these genes on kidney stone disease.

Results: This project helps us to inform the patient about the occurrence of mutations in the desired genes and the risk of developing kidney stone.

Conclusion: Our topic has not been evaluated by evaluating the common mutations with the investigated SNPs Rs200483989,Rs219780,RS1256328, congenital genetic disease of kidney stone in Tehran, and changing the genotypic structure in the mutations that occurred and evaluating the phenotypic evidence in kidney stone patients depending on the social genotype of a country. it must be done

Keywords: Kidney stone- SLC3A1,CLDN14,ALPL genes-SNP

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Investigating the effect of common mutations of SUGCT, TRPM8 and UFL1-AS1 genes in migraine patients in Tehran (Review)

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Introduction: Migraine continues second among the world's causes of disability. Diagnosis is based on the history and clinical examination and imaging is usually not necessary. Migraine can be subdivided depending on whether there is an aura or not and based on the frequency of the headaches. The number of headache days determines whether the patient has episodic migraine or chronic migraine. Most people who have migraines feel that people who do not have them often underestimate their condition. Migraines affect people's quality of life and ability to participate in work, family, and social events Typical aura without headache is a known entity within the spectrum of migraine. Its pathophysiology is suggested to be similar to classic migraines, with cortical spreading depression leading to aura formation but without an associated headache. No clinical trials have been performed to evaluate treatment options, but case reports suggest that most patients will respond to the traditional treatments for migraine with aura. Bilateral greater occipital nerve blocks may be helpful in aborting migraine with prolonged aura. Preventive therapy may also improve quality of life and prevent the progression to chronic migraines. Some indications for preventive therapy include four or more headaches a month, eight or more headache days a month, debilitating headaches, and medication-overuse headaches. Identifying and managing environmental, dietary, and behavioral triggers are useful strategies for preventing migraines. Migraine is a complex brain disorder that is explained by the interaction of genetic and environmental factors. Migraine is the third leading cause of disability worldwide, leading to reduced quality of life and serious economic consequences Genome-wide association studies have identified several susceptibility variants that confer only modest increases in the global risk of migraine. Genetic studies have

also shown the importance of common genetic factors between migraine and diseases such as depression and high blood pressure. There are 4 types of migraine headaches: frontal, temporal, occipital and rhinogenic.. Migraine is a common neurovascular disorder that affects 10–20% of the world's population, commonly divided into migraine with aura (MA) and migraine without aura (MO). Several GWAS have been performed in migraine. In a GWAS, several million common DNA variants, so-called single nucleotide polymorphisms (SNPs) scattered throughout the genome, are tested in large groups for association with a trait. Our aim is to investigate the SNP in the common genes TRPM8, SUGCT, UFL1-AS1, which causes early diagnosis in people with migraine disease and helps to improve these people in the society. Our subject by evaluating the occurrence of common mutations with the examined SNPs (13208321RS4379368, RS10166942, RS (genetic disease)

Methods: Using the PCR technique, The primary purpose of polymerase chain reaction (PCR) is to rapidly make many copies of a specific region of DNA or RNA so that it can be adequately identified, often by agarose gel electrophoresis. PCR is commonly used to amplify, modify and clone genes for expression studies. There are many uses for PCR, including paternity testing, biological relationships, mouse genotyping, diagnosing genetic diseases, forensics, and finding bacteria and viruses. we check the SNP sequences of TRPM8, SUGCT and UFL1-AS1 genes ،Single nucleotide polymorphisms (SNPs) are DNA sequence changes that occur when a single nucleotide in the genome is different in paired chromosomes. Some SNPs change the amino acid sequence of a protein in the coding region, and others in the coding region. , do not affect the protein sequence. SNPs outside the coding region may also affect transcription factor binding, gene splicing, or mRNA degradation. With or without such effects on the biological function of gene products, SNPs serve as markers for investigating imbalances. Linkage and detection of genetic polymorphisms are very useful in population genetics research and medical sciencewith gene expression , and by observing the electrophoresis gel, we find out the effect of gene expression and mutation of these genes on migraine disease.

Results: This project helps us to inform the patient about the occurrence of mutations in the desired genes and the risk of developing migraines.

Conclusion: Our topic has not been evaluated by evaluating the common mutations with the investigated SNPs RS10166942, RS4379368, RS13208321, congenital genetic disease of migraine in Tehran, and changing the genotypic structure in the mutations that occurred and evaluating the

phenotypic evidence in migraine patients depending on the social genotype of a country. it must be done.

Keywords: Migraine,TRPM۸,SUGCT,UFL۱-AS,SNP

Investigating the effect of curcumin on cisplatin-induced pancreatic toxicity in rats (Research Paper)

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Introduction: Cisplatin (CP) is an influential chemotherapeutic agent in the treatment of several types of malignant solid tumors, but its clinical use is related to pancreas toxicity. curcumin (CUR) is a natural antioxidant and scavenging free radicals. Here, we first explore the efficacy of CUR in the pancreas against the toxicity of CP and also analyze its mechanism.

Methods: Twenty-four Sprague-Dawley rats were equally divided into 3 groups, including, the control group which received only normal saline; the CP group which received only one dose CP (7 mg/kg/day) intraperitoneally (i.p.) for 24 h, groups treated with doses of 200 mg/kg/day CUR i.p. for 7 days, and the group treated which received the same dose of CP with doses of 200 mg/kg/day CUR i.p. for 7 days. After the treatments, animals were sacrificed. The malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) levels were evaluated in the pancreas. The histopathology of the pancreas was examined using hematoxylin-eosin. The serum was provided to assess Inflammatory factor (tumor necrosis factor (TNF)-alpha) and the lipase and amylase values.

Results: The results showed that CP significantly increased the level of MDA in tissue as compared to the control group. Moreover, severe tissue damage was detected in the pancreas. Whereas CUR significantly decreased the level of MDA. The activities of CAT, GSH-Px, and SOD in the pancreas tissues of the rats injected with CP were significantly lower than their activities in the control group. However, treatment with CUR in animals co-treated with CP resulted in a significant increase in the activities of pancreas tissues, when

compared to the CP-treated group. In the CP group, the levels of amylase and lipase increased compared with the control group. However, there were statistically significant differences among the CP group and the CP+ CUR groups in the values of both amylase and lipase. Serum TNF-alpha concentration in the CP+ CUR group significantly decreased compared with that in the cisplatin group. In addition, histopathological findings observed in the CP group in the pancreatic tissue alleviated in CP+ CUR groups.

Conclusion: These results indicate that curcumin acts to reduce cisplatin-induced pancreatic toxicity through its anti-inflammatory effects. Thus, curcumin may become a new therapeutic candidate for the treatment of cisplatin-induced pancreatic toxicity.

Keywords: Antioxidant activity, cisplatin, histopathology, curcumin, pancreas

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Investigating the Effect of Cytokine TNF-α on Tumor Cell Proliferation and Metastasis: A Preclinical Study and Systematic Review (Review)

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Introduction: Introduction: Thyroid hormones exert multiple effects on the testis and influence various cell types, including Leydig, Sertoli, and germ cells. Thyroid hormone deficiency can lead to testicular dysfunction, which manifests as abnormalities of seminal fluid. This systematic review in conjunction with a meta-analysis attempts to compare hypothyroidism with semen quality parameters that include sperm count, motility, and morphology.

Methods: MATERIALS AND METHODS: A comprehensive literature search was conducted to identify appropriate studies in PubMed, Scopus, Embase, and Web of Science databases, without geographic or language restrictions. Seven studies that met the eligibility criteria were selected, and the collected data were analysed using Comprehensive Meta-Analysis V3 software for meta-analysis.

Results: Findings: Ultimately, 7 studies with a total of 3497 participants were included. Cases of subclinical hypothyroidism had statistically significant reductions in total sperm count (SMD: -0.75, 95% CI: -1.29 to -0.21), normal sperm morphology (SMD: -0.99, 95% CI: -2.12 to -0.12), and progressive sperm motility (SMD: -1.56, 95% CI: -2.78 to -0.34) compared to control groups.

Conclusion: CONCLUSION: Consequently, scientific evidence supports the claim that semen quality parameters change in patients with hypothyroidism compared to their healthy counterparts. Thus, independent of other factors, hypothyroidism may play a crucial role in altering spermatogenesis and contribute to male infertility.

Keywords: Keywords: Hypothyroidism, thyroid hormones, semen analysis, sperm motility, semen quality.

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Investigating the effect of Echinacea purpurea on Nrf2 in Multiple Sclerosis by molecular docking method (Research Paper)

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Introduction: Multiple Sclerosis (MS) is a chronic neuroinflammatory disease occurring in the central nervous system (CNS), characterized by demyelination, axonal degeneration and inflammatory lesions. Invading leukocytes produce exorbitant quantities of cytotoxic mediators, including reactive oxygen species (ROS), which shift the oxidant/pro-oxidant balance. In order to counteract these devastating effects, the nuclear factor erythroid 2-related factor 2 (Nrf2) plays a pivotal role in advancing defenses. Several studies have indicated that within MS lesions, Nrf2 is upregulated in macrophages and astrocytes, therefore, the expression of several antioxidative enzymes is also elevated. Echinacea purpurea, commonly known as purple coneflower, contains substances that have shown promising effects on inflammatory responses, as well as immune cell functions. Furthermore, derivatives of this plant act as modulators in neuroprotective pathways that may be involved in pathogenesis of MS. The objective of this study is to evaluate the binding affinity between Echinacea purpurea and Nrf2. It is expected that if they establish a strong connection, Echinacea purpurea is likely to promote the activation of Nrf2, subsequently reducing oxidative stress in MS.

Methods: In this research, initially, the Nrf2 structure was obtained from the Uniprot website, then necessary preparations, such as adding charge and hydrogen ions, were performed using Chimera software. The three-dimensional structure of the Echinacea purpurea was downloaded from the PubChem website. The binding site of the DISC1 protein was determined using Deepsite. [Center; X: 38.518, Y: -11.120, Z: 3.625 and Dimensions (Angstrom); X, Y, Z: 25.00] Finally, the molecular docking process was conducted using AutoDock Vina in PyRx 0.8 to assess the binding status of Echinacea purpurea to Nrf2.

Results: Following the completion of the docking process of Echinacea purpurea and Nrf2, using PyRx software, the obtained results are as followed. For each model, the data belongs to their binding affinity, RMSD lower bond and RMSD upper bound, respectively: Model #1: [-8.9, 0.0, 0.0] Model #2: [-8.9, 1.425, 2.595] Model #3: [-8.5, 3.122, 9.59] Model #4: [-8.4, 1.545, 2.931] Model #5: [-8.1, 3.421, 9.413]

Conclusion: Based on the results of the molecular docking analysis of Echinacea purpurea and Nrf2, it was determined that in accordance with the negative binding energy, Echinacea purpurea can bind well to Nrf2. The efficacy of Echinacea purpurea in MS treatment requires further investigation; however, current research shows possibilities for utilizing this herbal medicine by targeting Nrf2 signaling pathways, due to its good binding status.

Keywords: Echinacea purpurea, Nrf2, Molecular docking, Multiple Sclerosis, oxidative stress

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Investigating the effect of L. edodes on viral immunity caused by influenza pneumonia caused by it (Research Paper)

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Introduction: This is a virus from the Orthomyxoviridae family that causes many symptoms of the common cold. The RNA influenza virus is a severe respiratory infection that mostly affects people during the winter season, and many of the deaths we witness annually are caused by its growth and transmission, resulting in pneumonia and death. Symptoms of this disease range from high fever and headache to nasal congestion, sore throat, chest pain, severe malaise, and pneumonia. The incidence of the disease can occur from contact with aerosols from infected individuals in the case of swine and avian flu, or from exposure to contaminated animals. Shiitake mushroom is an edible fungus that its active ingredient, AHCC, grows in China and Japan and is now available worldwide as a viral and bacterial disease inhibitor and immune system booster in the form of tablets. The aim of this study is to confirm the antiviral and antibacterial process of this type of mushroom in acute influenza in Syrian rats. In this research, after infecting a rat with the flu and confirming it, the rats were divided into two groups: control and treated with shiitake mushroom extract. The results clearly showed that the recovery rate in the group treated with shiitake mushroom extract was significantly higher than the control group, which received distilled water.

Methods: We collected 800g of raw shiitake mushroom and dried it using indirect heat in a sterile autoclave. We extracted the essence using a Soxhlet extractor and concentrated it to a volume of 200ml using a rotary evaporator. The concentrated extract was kept in the dark at 20°C. We separated 40 male Syrian mice weighing 300g each and injected them intraperitoneally with a standard strain of influenza type C and Streptococcus pneumoniae. They were randomly divided into two groups of 20 and marked accordingly, then kept in cages. After verifying the presence of influenza and pneumonia symptoms with an electronic thermometer, we began treatment with the shiitake mushroom extract. The rats were given the extract three times a day in doses of 2.5ml, 3ml, and 5ml using a syringe. The control group received

the same dose of distilled water. After 21 days, we examined the important results and recorded them in a table.

Results: Based on the results obtained from this study, it can be stated that this type of edible mushroom can be one of the most helpful medications for controlling and even treating severe influenza, and can potentially cure it. Given the indiscriminate use of antibiotics and self-medication, it would be better for doctors to prescribe mushroom extract powder and even edible mushrooms as one of the strongest antiviral and antibacterial substances, instead of prescribing antibiotics and antihistamine drugs.

Conclusion: Based on the results of this study, it can be inferred that this type of plant can be a useful therapeutic aid for severe cases of influenza. Additionally, Dr. Anderson demonstrated its antiviral and anti-inflammatory properties through research conducted in 2020 (16). Professor Koda confirmed the antiviral activity of this fungus in a separate study, and in 2023, Ahmad also confirmed its antiviral effects (17). Furthermore, Dr. Young examined and confirmed the anti-inflammatory effects of this substance in 2022.

Keywords: Shiitake, pneumonia, mushroom , viral infection , traditional medicine

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Investigating the effect of lncRNA H19 on CST2 and GJB2 expression in breast cancer (Research Paper)

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Introduction: Breast cancer is the most commonly occurring cancer in women. Long noncoding RNAs (lncRNAs) are noncoding transcripts with more than 200 nucleotides such as antisense RNAs, enhancer RNAs, and endogenous RNAs. lncRNAs can help as a tumor suppressor and oncogenes to cell growth, metabolism, and metastasis. Long non-coding RNA H19 is abnormally expressed in some types of cancers. Previous studies have shown the effects of H19 on breast cancer development, metastasis, and progress. Changes in the expression of CST2 and GJB2 genes have been reported in the early stages of tumorigenesis so that these two genes can be used as diagnostic markers. Therefore, the aim of this study is to investigate the expression changes of CST2, and GJB2 in patients with breast cancer and the effect of long non-coding RNA H19 on CST2, and GJB2 expression levels by bioinformatics approaches.

Methods: in this study, we used the GEO website (https://www.ncbi.nlm.nih.gov/gds) to find access codes related to Breast cancer. Also, to quickly access we used filters including Homo sapiens, series, and expression profiling by the array. The differentially expressed genes (DEGs) were identified using the GEO2R tool. Finally, investigating the effect of lncRNA H19 on CST2 and GJB2 expression was studied by lncRRisearch.

Results: We used GSE42568 for Breast Cancer Gene Expression Analysis, 104 breast cancer biopsies were studied in this microarray gene expression datasets. 11 samples with grade 1; 40 samples with grade 2; 53 samples with grade 3, and 17 normal breast tissues were assayed in GSE42568. The GEO2R tool (cut-off value: 1 and p-value < 0.05) showed that GJB2 with Logfc: -2.89 and CST2 with Logfc: -1.54 were down-regulated genes. In lncRRisearch results, the energy interaction of GJB2-H19 and CST2- H19 was -16.66 kcal/mol and -19.97 kcal/mol, respectively.

Conclusion: Our insilico study showed that H19 is involved in changing the gene expression profile of GJB2 and CST2.

Keywords: lncRNA, Breast cancer, GJB2, CST2, H19

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Investigating the effect of radiotherapy and sonodynamic therapy in the presence of nanoparticle on breast cancer cells (Research Paper)

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1.
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Introduction: Introduction: Sonodynamic therapy and nanoparticles with green compounds, along with radiotherapy, could reduce complications and improve the treatment of cancer. This study aimed to investigate the efficacy of low-dose radiotherapy and sonodynamic therapy in the presence of apigenin-coated gold nanoparticles on the breast cancer cell.

Methods: Methods and materials: The synthesized apigenin-coated gold nanoparticles were confirmed by UV-visible, HR-TEM, DLS, zeta-potential, and FTIR. Ultrasound parameters were estimated at the acoustic cavitation threshold by mechanical index modeling. The toxicity of the nanoparticles and methylene blue were evaluated by MTT. The concentration of apigenin-coated gold nanoparticles was measured, and they were then irradiated by ultrasound and 2 Gy x-ray radiation.

Results: Results: Ultrasound with a mechanical index of 0.40 was estimated at a distance of 2 cm from the 1-MHz transducer with 2 W/cm2 in the continuous mode. The MTT assay indicated that sonodymic therapy combined with radiation therapy at the concentration of 8 µg/ml nanoparticles significantly affected cell death (0.26± 0.02).

Conclusion: Conclusion: Using sonodynamic therapy as a non-invasive and non-ionizing treatment with novel sensitizers based on optimum physical parameters can increase cell death in low-dose radiation therapy.

Keywords: Keywords: Sonodynamic therapy, Radiation therapy, Apigenin-coated gold nanoparticles, Viability

Investigating the effect of silver nanoparticles on the disease (Research Paper)

hossein ameri shahrabi,[1,*]

1. Education and training

Introduction: Title: Investigating the Effect of Silver Nanoparticles on Disease: An Overview and Research Methodology Introduction: In recent years, nanotechnology has emerged as a groundbreaking field with vast potential for applications in various sectors, including medicine. Silver nanoparticles (AgNPs) have garnered significant attention due to their unique properties, such as antimicrobial and anti-inflammatory capabilities. As a result, researchers have increasingly turned their focus toward investigating the potential therapeutic effects of AgNPs on various diseases. This article delves into the intriguing world of AgNPs and presents a research methodology for studying their impact on disease. Silver Nanoparticles: A Brief Overview Silver nanoparticles, typically ranging in size from 1 to 100 nanometers, exhibit exceptional physicochemical properties. These properties include a high surface area-to-volume ratio, exceptional electrical and thermal conductivity, and a unique optical response. However, one of the most noteworthy characteristics of AgNPs is their potent antimicrobial activity. This property has been exploited in various medical applications, from wound dressings to catheters, to combat infection and enhance healing. Research into the therapeutic potential of AgNPs has expanded beyond their antimicrobial properties. It is now widely recognized that these nanoparticles possess immunomodulatory, anti-inflammatory, and antioxidant effects, making them promising candidates for the treatment of a wide range of diseases, including cancer, neurodegenerative disorders, and autoimmune conditions.

Methods: Selection of Disease Model: To investigate the effect of silver nanoparticles on a specific disease, it is essential to select a suitable disease model. The choice should be based on the disease's prevalence, relevance to AgNP properties, and ethical considerations. Synthesis and Characterization of Silver Nanoparticles: Synthesize AgNPs using a well-established method, such as chemical reduction or green synthesis. Characterize the nanoparticles' physicochemical properties, including size, shape, surface charge, and stability, using techniques like TEM, SEM, XRD, and zeta potential analysis. In Vitro Studies: Conduct preliminary in vitro studies to evaluate the cytotoxicity of AgNPs on relevant cell lines. Assess the nanoparticles' effects on cellular processes, such as inflammation, oxidative

stress, and apoptosis, using molecular and biochemical assays. Animal Model Studies: If applicable and ethical, proceed to animal model studies. Select an appropriate animal model that mimics the disease characteristics in humans. Administer AgNPs through various routes, considering factors like dosage, frequency, and duration. Monitor disease progression, histopathological changes, and immune responses in treated animals. Bioavailability and Biodistribution: Determine the bioavailability and biodistribution of AgNPs in the body using techniques like ICP-MS and fluorescence imaging. Data Analysis: Analyze the data using statistical methods to determine the significance of the observed effects. Consider potential confounding variables and control for them in the analysis. Ethical Considerations: Ensure that all research involving animals or human participants adheres to ethical guidelines and obtains necessary approvals from relevant ethics committees. Conclusion and Future Directions: Summarize the findings and their implications for the treatment of the investigated disease. Discuss potential limitations and avenues for future research. In conclusion, the investigation of silver nanoparticles' effects on diseases holds great promise for advancing our understanding of their therapeutic potential. Properly designed research methodologies are crucial to ensure robust and reliable results that can ultimately contribute to the development of innovative treatments for various diseases.

Results: Investigating the effects of silver nanoparticles on diseases holds great promise for advancing our understanding of their therapeutic potential. Properly designed research methods are crucial to ensure robust and reliable results that can ultimately contribute to the development of innovative treatments for various diseases.

Conclusion: Investigating the effects of silver nanoparticles on diseases holds great promise for advancing our understanding of their therapeutic potential. Properly designed research methods are crucial to ensure robust and reliable results that can ultimately contribute to the development of innovative treatments for various diseases.

Keywords: Investigating the effects of silver nanoparticles-silver nanoparticles

Investigating the effect of stem cells on the treatment of rheumatism (Review)

Maedeh jamshidian,[1,*]

1.

Introduction: Rheumatism is a disease that affects muscles, joints, and bones, and this problem causes inflammation, pain, and other types of problems, although doctors have not yet determined the main cause of the disease, some of its causes can be identified: Genetic factors, incorrect lifestyle, metabolic problems, nervous system problems, etc. were considered. Nowadays, doctors try to stop the progress of this disease by prescribing various drugs and control it temporarily. A person who gets this disease may even be unable to do his daily tasks due to the pain caused by this disease. And on the other hand, the many side effects of the drugs used by these patients make for difficult and exhausting days for them. So, every person suffering from this disease is undoubtedly looking for pain relief and using an effective treatment method with less side effects. Recently, in country of Iran, scientists have succeeded in producing a medicine using stem cells, which is a cure for many difficult diseases, such as rheumatism and arthritis. Therefore, this research was conducted with the aim of investigating the effects of stem cells on the treatment of rheumatism, and the results and stages of this research can be seen in article.

Methods: This article is a review and field and library methods have been used

Results: From this research, we can reach the conclusion that stem cell is a cure for many diseases and it is an emerging science in the world that many treatments will be based on in the future, these cells that have the capabilities and abilities they have a unique feature that distinguishes them from other cells. But this unique science is still unknown among some people, or if they know it, it is not completely. Rheumatism and joint diseases are among the diseases that did not have a definitive treatment before stem cells, and even if there was something called a treatment, it would only temporarily relieve pain or inflammation, and none of them were definitive, that's why with the development of Kimiacell medicine By Iranian researchers, hope was revived in the hearts of rheumatic patients for recovery And without a doubt, with this drug, which is a more definitive and effective method, many severe joint diseases can be treated.

Conclusion: What is rheumatism? Rheumatism is the most common joint disease, which is caused by several factors. Such as: age, sex, genetics, bone density, major joint injuries, lifestyle, etc. can be considered as one of these factors [1]. The most important problem in this disease is the excruciating pain of the affected patient and the lack of medicine and definitive treatment. and there are only medicines that slow down the progress of the disease and relieve the patient's pain, but all of them are temporary and have many side effects, and if the patient stops taking his medicine even for a week, all kinds of joint pains will come to him[5]. This has led to an increase in knee joint replacement surgeries and the use of various drugs, and it is clear that the existence of a safe, effective and cheaper treatment that can change the course of the disease will have a significant impact on life and treatment costs in the future [2]. Treatments based on stem cells and cartilage tissue engineering have created new ways to treat this disease, as a biological therapeutic agent for the treatment of inflammatory diseases and tissue repair [1]. Types of rheumatism treatment Home treatment is one of the methods that is based on traditional medicine and is effective in reducing joint rheumatism pain. For example, using vegetable oils such as olive oil, chamomile, etc. Sleeping with it and massaging the pain area, or using warm teas such as ginger with black pepper, honey and black seeds are only a small part of the traditional medicine treatment methods, but none of them are definitive treatments and only relieve the pain for a short time. Gives [4]. Taking drugs such as: painkillers, non-steroidal anti-inflammatory drugs. Most people with rheumatoid arthritis need to take more than one drug, and the amount of these drugs varies depending on the symptoms because each one works in different ways [3]. Surgery is another way of treatment. If joint pain and inflammation become unbearable or if they are seriously damaged, parts such as hip, knee and sometimes shoulder joints may need to be replaced [2]. Occupational therapy and physical therapy are other methods of treatment that are very effective and help to improve the condition of the patient and improve the quality of daily work with exercise. Treatment with physiotherapy and acupuncture, which reduces swelling and pain and is effective in strengthening the immune system of the affected patient, is also one of the other methods of treatment [8]. Each of the ways to treat this disease have side effects and benefits, and the most important thing about these methods is that the treatment is not definitive, which is important and noteworthy because the patient spends a long time for each of the above methods. Again, he recovers for a short period of time and after a while, chronic pains come back to him, so the existence of an effective method for these patients is very important because none of the people suffering from this disease is willing to take several pills and drugs with high side effects for They don't last long and they are looking for more effective and better ways to treat their disease. On the other hand, the variety of treatment methods and, accordingly, the high

cost of each treatment method annoys patients. Therefore, even though stem cell is a new and almost unknown treatment method among these patients, it has been the most effective method [9]. What is a stem cell? The building block of the body of any organism is called a cell. All cells do not have the same function and shape, and the types of cells include: nerve cells (neurons), muscle cells (myocytes), skin cells (epithelial cells), blood cells and bone cells (osteocytes), cartilage cells. It is "chondrocytes" [3]. The origin of all these cells is the egg cell, which after multiple divisions and differentiation of the resulting cells, leads to the formation of the living body [5]. The stem cell is called the mother of all cells. Due to the unique abilities of stem cells, these cells are considered popular and attractive topics in biology and medical sciences today [6]. These cells have the ability to transform into all kinds of cells, including blood cells, heart cells, nerve cells, cartilage cells, etc. They also play a role in repairing damaged tissues and fixing defects in that tissue [3]. The human body consists of 200 different types of cells, and the task of building, supplying and maintaining cells is the responsibility of stem cells, and depending on the type of different tissues, they make up less than one to five percent of the cells of each tissue [2]. Types of stem cells There are types of embryonic, adult and umbilical cord blood stem cells, and the types of stem cells based on differentiation ability include: omnipotent, pluripotent, multipotent and monopotent. Omnipotent or embryonic cells are cells that are capable of becoming all cells, these cells can be obtained from four- or five-day-old embryos resulting from in vitro fertilization and grown in culture environments [7]. Pluripotent cells are cells that have already been affected by cell differentiation and can only divide and differentiate in a range of cells. Multipotent cells are a lower class of pluripotent cells and differentiate into cells related to a specific tissue. Unipotent cells have the lowest differentiation power and the greatest limitation among stem cells, and they only have the ability to make one differentiated cell[10]. The history of stem cells One of the most important applications of stem cells to date has been bone marrow transplantation. In the early 19th century, doctors prescribed bone marrow stem cells as food for patients with cancer or anemia. Although this method was never useful, researchers found that injecting bone marrow cells from a healthy mouse into the blood system of a mouse with a defective bone marrow can greatly help restore the bone marrow, and for this reason, the thought of bone marrow transplantation. They also fell in humans. Greppe performed several bone marrow transplants in France in the late 1950s, but bone marrow transplants were never performed on a large scale. Until 1958, a French researcher succeeded in discovering histocompatibility antigens in humans. These antigens, which are found on the surface of most body cells, increase the ability of the body's immune system to identify foreign cells [6]. The greatest scientific achievement in the field of stem cells was achieved in 1998. This year, Thomson and his colleagues were able to use five cell lines

from the blastocytes of human embryos. The cell lines obtained by Thomson and colleagues expressing stem cell markers had high telomerase activity, and their injection into immunosuppressed mice led to teratoma formation. Later studies on embryonic stem cells showed that these cells have the ability to differentiate into cells from all three embryonic layers: ectoderm, endoderm, and mesoderm, and it was found that these cells can have therapeutic potential. And they also have the ability to differentiate into dopamine-producing nerve cells [5]. Stem cell therapy Recently, the researchers of Royan Research Institute have succeeded in obtaining and making a drug using stem cells, which has been tested on knee joints and has been found to be effective. This method is much more effective in relieving pain and improving the patient than other methods. Success is effective for treating many difficult diseases such as: rheumatism, arthritis, arthrosis, etc. This drug is made under the name Kimiacell, which is suitable for all people without genetic compatibility.

Keywords: Stem cell, Rheumatism, Kimiacell drug, joints.

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Investigating the effect of tetracycline antibiotic on tetQ gene transfer (Research Paper)

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Introduction: The human intestine is a very suitable place for the growth and reproduction of its natural microflora, and in case of problems, it is the basis for the production of infection for pathogenic bacteria. Human gut bacteria have many roles in human health, most of which are beneficial or neutral to the host. Until recently, bacterial pathogens were the main focus of studies of antibiotic resistance genes and their spread. The possibility that resistance genes in the human colon may pose a serious threat to human health was first raised in connection with post-surgical infections, which are usually caused by the natural microflora of the patient or the patient's caregivers. The entry of uncooked food contains resistant bacteria in the intestine, which, if this happens, will be able to combine with the human microflora. At the same time, potentially pathogenic bacteria live in the intestine, such as Staphylococcus aureus and Escherichia coli, enterococcus species. , Clostridium species and Bacteroidetes species. In the study conducted on DNA sequences for resistance genes found in different bacteria in the human colon or in other places, it has been shown that if the genes found in two different bacteria species are at least 95% identical , this gene must have been transferred horizontally. To determine what type of element carries the tetQ sequence, the DNA of some strains carrying tetQ is examined with the DNA of a conjugative transposon known as tetQ, known as CTnDOT. The specificity of this sequence is that the transfer of CTnDOT and related conjugated transposons is stimulated 100-1000-fold by tetracycline. Therefore, the widespread transmission of tetQ, which has occurred over the past three decades, may have been caused by the use of tetracycline.Therefore, the widespread transmission of tetQ, which has occurred during the past three decades, may have been caused by the use of tetracycline. In another study, it was found that before the widespread use of tetracycline, the transfer of this gene in bacteria reached the rate of 20-30%. Meanwhile, studies on CTnDOT type element in 1990 showed that horizontal gene transfer even It happened before the intensive use of tetracycline. Early childhood antibiotic exposure is associated with immune, neurological, and gastrointestinal effects, and antibiotic use at any age is associated with negative effects on the gut microflora that lead to the emergence of Diarrhea becomes resistant to antibiotics, it is related. Gut microbiota also plays a role

in the activation and inactivation of drugs such as sulfasalazine, digoxin, irinotecan, chloramphenicol, and nitrobenzodiazepines

Methods: At first, stool samples were collected from Spain and the United States of America. In the sample that carries the bacteria in the aforementioned resistance genes, it was included in the known classification of resistance gene families. Therefore, based on the analysis of the number and types of microorganisms and their ability to resist, it was defined as the average fraction of the genome encoding resistance genes for a specific antibiotic or other antibiotics.

Results: According to the tests and the obtained results, it was found that in the presence of tetracycline antibiotic, there is a 100-1000 times probability of tetQ resistance gene displacement in the natural microflora, which indicates that under specific conditions, this antibiotic no longer has its lethality. and causes resistance in other species

Conclusion: With the widespread production of industrial and natural antibiotics, the resistance of the natural microflora of the body will increase to the same extent, and this is a serious risk for the health of humans and animals that use antibiotics for treatment. For this reason, using this medicine correctly can minimize the risk of antibiotic resistance.

Keywords: Tetracycline antibiotic. tetQ resistance gene. CTnDOT element

Investigating the effect of utilizing Lysis Buffer in the DNA extraction protocol of frozen blood (Research Paper)

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Introduction: Progress in any scientific field depends on the availability of new and advanced techniques and methods which are considered important for medical diagnosis tests in diseases that have a genetic origin and also for extracting DNA from blood and tissues. One of the problems that sometimes occurs with genomes in tropical regions is the freezing and unfreezing of old genomes, which can occur for various reasons: including power outages, hot weather and etc. This issue causes excessive fragmentation of the genome, which may lead to false results or no results in the research process; Therefore, in this article, an attempt has been made to investigate a better method for extracting the genome from frozen blood.

Methods: In this study, to achieve a better result, a total of 450 blood samples of the human genome that were frozen and refrozen at least four times were used. At first, these samples were extracted using the salting method and only water was used for washing. Again, they were extracted from blood cells using a lysis buffer with NH4Cl, NaHCO3 and EDTA compounds.

Results: Due to the use of lysis buffer instead of water, the washing rate of old genomes and centrifugation cycle (8500rpm) to separate nucleated cells was reduced and white Cells were observed earlier in the sediment. The need for vortex in different stages was also reduced and the amount of use of solutions of TES, SDS and proteinase k(Cinnagen) were also reduced, which were 300,25,20 µL respectively. Finally, The quality and quantity of extracted genomes were checked (figures 1, 2) Figure-1:Agarose gel electrophoresis (1%) with DNA extracted from blood samples Figure 2: Absorption diagram through nanodrop device

Conclusion: The physical as well as chemical treatments involved in DNA extraction can affect both the quantity and quality of the DNA obtained. In this regard, the present study showed that extracting DNA from old and broken blood samples requires great accuracy. For example, using the right

detergent to reduce the amount of washing, vortexing and centrifugation can reduce the amount of genome breakage and be effective in the quality and quantity of the extracted genomes.

Keywords: DNA extraction ;salting-out protocol; Genome; lysis Buffer

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Investigating the effects of increasing ROS during Cryopreservation technique on sperm quality (Review)

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Introduction: Today, infertility is a global problem that, in addition to economic costs, also has destructive effects on the mental health of couples. According to the World Health Organization (WHO), about half of infertility cases are caused by male factors. Due to the importance of the issue of infertility, various techniques have been proposed to help in the treatment of it. Sperm cryopreservation (SC) is one of the techniques used in infertility treatment centers and sperm banks, however, this method has destructive effects on sperm. One of the most important damages caused to sperm in this method is the increase in the production of reactive oxygen species (ROS). ROS include different types that through different mechanisms such as DNA damage, cell membrane, and other membrane organelles damage lead to a decrease in the chance of successful fertilization. Due to the importance of the infertility issue, in this review, first, the damage caused by ROS on the male reproductive system is discussed. Below is some information on the effect of antioxidants to help improve ROS levels in sperm.

Methods: An exhaustive literature review was conducted to assess original investigations. Relevant studies published between 1996 and 2023 were identified by searching the PubMed, Web of Science, and Google Scholar databases using keyword combinations related to male infertility, sperm, cryopreservation, oxidative stress, apoptosis, DNA damage, and signaling pathways. Inclusion criteria stipulated original research articles published in English that directly examined indicators of cryopreservation-induced damage and antioxidant efficacy in sperm samples. Additional applicable papers were identified by hand-searching the reference lists of reviews and included articles. Overall, articles met all inclusion criteria and were compiled to qualitatively summarize the evidence on mechanisms of cryopreservation damage, antioxidant mechanisms of action, and future directions to optimize sperm integrity during freeze-thaw procedures. This comprehensive review synthesizes current knowledge on pathways of sperm damage during

cryopreservation and the protective effects of antioxidant supplementation based on the past 3 decades of articles.

Results: After skimming and fully understanding the articles, this review found that the increase in ROS levels leads to increased oxysterol production and membrane permeability to cytochrome C. Additionally, it can elevate the production of procaspase 9, apoptotic bodies, caspase 3, and DNA fragmentation. Also, by activating the SIRT1/Nrf2 pathway and releasing cytochrome C from mitochondria, it decreased the expression of Bax and reversely increased the expression of Bcl-2. On the other hand, elevation of ROS can reduce the PI3K/AKT/mTOR pathway, induce NOX and CHAC1, formation of TNF, and induction of NF-kB, which has harmful results (e.g., cell damage, apoptosis, mitochondrial activity impairment, DNA damage, inhibition of sperm motility, sperm morphology alteration) on spermatogenesis. As an attachment for the review, various antioxidants including vitamins C and E were traced. Many studies have shown the role of various antioxidants and have confirmed the effective removal of ROS through the reduction of malondialdehyde production and lipid peroxidation.

Conclusion: This literature review demonstrates that SC leads to elevated ROS levels, which induces pathological changes through diverse molecular pathways. The increased ROS prompts oxysterol production and membrane permeabilization, enabling the release of apoptogenic factors like cytochrome C from the mitochondria. ROS activates caspase cascades (caspase 9, caspase 3) and nuclear fragmentation, culminating in apoptotic sperm death. However, the stimulation of cytoprotective mechanisms like the SIRT1/Nrf2 pathway and enhanced Bcl-2 expression can counteract apoptotic signaling. Conversely, ROS impairs sperm function by reducing PI3K/AKT/mTOR activity, inducing expression of pro-oxidant enzymes (NOX), and damaging DNA integrity. Additional deleterious effects include impaired sperm motility, aberrant morphology, and inhibition of mitochondrial activity. These pathological effects are mediated through ROS-induced signaling molecules like CHAC1, TNF, and NF-kB. Numerous antioxidants have proven effective at mitigating ROS-induced damage by reducing lipid peroxidation and oxidative stress. For instance, supplementation with vitamin C and vitamin E decreased malondialdehyde levels, confirming their role as ROS scavengers. In summary, this review elucidates the diverse molecular cascades through which accumulated ROS during cryopreservation adversely impact sperm viability and function. It also verifies the protective capacity of antioxidant molecules to preserve sperm from oxidative damage. Further research should explore combinatorial antioxidant therapies to optimize sperm integrity and mitochondrial health during cryopreservation procedures.

Keywords: Male infertility, DNA, Oxidative stress, Sperm Cryopreservation

Investigating the effects of nanotechnology in the process of cancer treatment (Review)

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1.

Introduction: Today, cancer is one of the most important causes of death in the world. Cancer is a disease in which some cells in the body begin to divide and multiply without stopping and they penetrate the surrounding tissues and begin to spread. In the normal state of the body, cells grow and divide to from the cells the body needs, Then, when these cells get old or damaged, a new cell takes their place. When cancer occurs, this process breaks down and a tumor is formed by dividing and multiplying cells without stopping. Today's common treatment methods have problems, For example, in the treatment of cancer, due to the limited access of drugs to the cancerous tissue, it may also damage healthy cells and cause many losses and on the other hand, the appropriate does of medicine does not reach the cancer cell. With the advancement of nanotechnology, this problem can be completely solved. By using nanoparticles, it is possible to target and accurately deliver the drug only to the cancer tissue and cell, which reduces the possible damage to the healthy cell to zero. With the invention of nanorobots, a treatment of cancer. Nanorobots deliver drugs to cancer cells, by penetrating the cancer cell, they destroy it! And by sensitizing the cancerous tissue, they cause accurate imaging of the tissue. Therefore, nanotechnology creates a big revolution in cancer treatment.

Methods: This article is a review and field and library methods have been used

Results: Conclusions can be drawn from these studies. Cancer is a common disease that causes death in the world, Although today's treatment methods slightly prevent cancer progression, there is still no effective and useful method with the least damage. But nanotechnology has provided useful methods and solutions with minimal damage. Because drug transfer in therapeutic methods is not targeted, it may also damage healthy cells and tissues, and this problem is solved with nanoparticles. Although they are very small, they penetrate into the cancer cells and deliver drugs only to the cancer cells in a targeted way, which reduces the damage of the treatment methods. Chemotherapy is one of the most widely used methods for cancer treatment, but chemotherapy drugs are undesirable due to side effects and high toxicity sine these drugs do not target the cancer cell, this problem can be solved in

chemotherapy with nanoparticles. Radiation therapy also has disadvantages, For example, exposing the body to high-energy radiation causes problems that, if radiation therapy is combined with nanotechnology, will have a significant impact on cancer treatment. Also, with the invention of nanorobots, a huge revolution was created in cancer treatment. These nanorobots can be easily used for drug delivery. It also examines the cancerous tissue and finally causes the destruction of the cancerous tissue and destroys the cancerous cells, which greatly increases the probability of survival of people with cancer. Today, scientists are focusing on various methods based on nanotechnology to provide new and potential ways to treat cancer. In fact, it can be said that the combination of nano science with cancer treatment methods can create a miracle in the treatment and recovery of patients suffering from all types of cancer.

Conclusion: What is cancer? Cancer is one of the common diseases that affects many people around the world. Cancer is one of those diseases that starts in one part of the body and if it is diagnosed late, it spreads throughout the body and affects all the important organs of the body. In fact, cancer is a disease in which some cells in the body begin to divide without stopping and penetrate and spread to the surrounding tissues (2). In the normal state of the body, the cells of the body grow and divide to form new cells that the body needs. Then when the cells get old, they die and a new cell takes their place. When cancer occurs, this process is broken and old or damaged cells survive when they should be killed, then begin to divide and multiply and may lead to tumor formation (3). Many cancers have solid tumors, but blood cancers like leukemias don't produce solid tumors (6). Cancerous tumors are either malignant or benign, malignant tumors mean that the cancer cells in the tumors tissue can invade the surrounding tissues and then spread and on the other hand, the location of malignant tumors is sensitive and the surgery of this type of tumor is very sensitive and risky, and even if the malignant tumor is surgically removed, there is a possibility of its regrowth (3). While a benign tumor doesn't invade surrounding tissue, it doesn't spread to nearby tissues, and if benign tumors are removed, they will not grow back, and the surgical risk of benign tumors is often lower than that of malignant tumors (3). How does cancer accur? Cancer is genetic disorder, that is, it's caused by the change of genes in the cell that control the function of the cells, especially the way they grow and divide (7). Genetic changes that cause cancer may be inherited from parents. It's also possible that the environmental factors that a person has encountered during her or his life can cause genetic disorders and cause cancer. Environmental factors such as chemicals in tobacco and UV rays 6 from the sun. For example, people who use drugs may increase their risk of cancer by several percent (6). When does cancer spread in the body? If cancer starts from one place and spreads to other parts of the body, it's

called metastatic cancer, and the process that causes cancer to spread in the body is called metastasis (4). Metastatic cancer cells look similar to primary cancer cells under the microscope and both have some molecular features such as chromosomal changes. The overall goal of treating metastatic cancer is to control the growth of the cancer or to relieve the symptoms caused by the cancer. Metastatic tumors cause severe damage to the immune system. Therefore, most of the people who die from cancer, metastatic cancer is the cause of their death (5). How to diagnose cancer Cancer diagnosis requires physical tests, if cancer is detected in time, it can be prevented from spreading and affecting the important organs of the body (3). Some of the cancer diagnosis methods include the following; 1- Laboratory tests , 2- Diagnosis imaging , 3- Genetic tests , 4- Tumor sampling (4). Cancer treatment methods Cancer treatment depends on the type, location and extent of its spread in the body. Cancer treatment methods aim to improve the patient's condition or prevent cancer progression. According to the patient's condition, one or two methods are used in combination for treatment. Methods include the following: 1- Surgery 2- Chemotherapy 3- Radiotherapy 4- Immunotherapy 5- Hormone therapy (9). 7 Nanotechnology in cancer treatment Chemotherapy is one of the well-known methods for treating cancer patients. But cancer treatment has not been very successful due to the limited access of drugs to cancer tissue, intolerable toxicity and multiple drug resistance. In recent years, due to the better understanding of tumor biology and the advancement of nanotechnology, new solutions for cancer treatment have been presented. Nanoscale particles act in surprising ways (10). So that the properties and characteristics of materials change on a nanometer scale and they show special optical, electronic and structural properties. It was the first nano cancer drug approved by the US Food and Drug Administration. Since 1995, it has been used to treat adult cancers, including ovarian cancer, multiple myeloma, and sarcoma { A rare cancer that often affects immunocompromised patients such as AIDS patients.} is used (5). It's possible that common and classic cancer treatment risk damaging healthy tissues. In fact, to destroy the cancer cells, the rest of the healthy tissues are forcibly affected (3). Scientists are currently working on nanotechnologybased cancer treatment to overcome this limitation and increase the likelihood of healthy tissue survival in several types of cancer (4). How nanotechnology affects cancer treatment? By delivering the drug to the specific target of cancer cells, nanotechnology improves current treatment methods such as chemotherapy and reduces its adverse effects (10). Also, surgery to remove tumors is done with much more precision. The effectiveness of radiotherapy and many common treatment methods increases. Researchers are developing therapies with newly discovered nanoparticles that have new properties for use in medical science. While nanoparticles are very small in size, they contain small amounts of medicinal compounds (6). As a result,

things like combination drug delivery, multimodality therapy, and theranostic performance {combination of therapy and diagnosis} become easy. The energy absorption and 8 reradiation properties of nanoparticles also help them improve laser and hyperthermic applications that disrupt diseased tissue (9). Drug delivery with the help of nanoparticles The main application of nanotechnology in oncology is drug delivery. A lot of research shows that nanotechnology is successfully used to design many systems. These systems limit the side effects of drugs and increase the patient's chances of health (2). They also allow chemotherapy to be more selective, thus delivering drugs to specific tumor tissues. This methods involves the development of nano sized carriers that deliver the drug to its target {Figure1}. In animal studies, this system has been shown to be effective in delivering capecitabine to diseased cells while bypassing healthy cells. This reduces side effects and increases the efficiency of the tumor reduction activity (5).Strengtheningi mmunotherapy with nanoparticles Another encouraging area of nanotechnology in oncology is the enhancement of immunotherapy. While immunotherapy was previously recognized as an exciting and 9 potentially very effective treatment option for the treatment of various types of cancer, However, the proportion of patients who respond positively to immunotherapy is low, with only 15% of patients showing an objective response rate across symptoms. This is related to multiple methods of tumor immunity (11). To optimize the efficiency of the immune system against cancer, nanotechnology is used to manage the spatial and temporal control of the immune system(7). Nanotechnology and immunotherapy Immunotherapy is performed in about half of cancer patients during a treatment period. In immunotherapy is effective in reducing the size of tumors by exposure to high energy rays. However, these rays can also damage healthy cells(5). Scientists are working on increasing the effect of radiationtherapy and developing new electromagnetic radiation. The combination of nanotechnology and immunotherapy produces more effective results than immunotherapy alone(10). Nanorobot Recent successes in targeted cancer therapy have led to the invention of nanorobot molecular machines. Nanorobots have revolutionized the diagnosis and treatment of cancer. Nanorobots are made of organic and intelligent materials that are programmed into units through genetic embedding of their constituent structures (10). Most nanorobots consist of a sensing agent and a cytotoxic agent. The sensor agent can consist of one or more chemical strands, each of which is activated by a specific agent in the target cell. These nanorobots consist of a gold nanoshell, an antibody fragment, and an aptamer sensing agent. An agent is a molecular sensor that recognizes antigens on the surface of certain cancer cells (9). After identifying the cancer cells, its contents are dissolved and the loaded substances penetrate into the cancer cells and destroy 11 the cancer cells. Recently, nanorobots have been designed as an intelligent drug delivery system (10). When the nanorobot is in close proximity

to cancer cells, it triggers the release of thrombin, which causes blood to clot at the tumor site and finally, it causes tumor necrosis and inhibits the growth of cancer cells(9).New solutions for the treatment of cancer stem cell In the current treatment of cancer, the issue of drug resistance leads to the accumulation of cancer stem cells and the recurrence of treated tumors. Various solutions have been proposed for the treatment of cancer, the most important of which is the use of drug delivery systems based on nanoparticles (2). These solutions can be divided into three main categories: 1-Targeted drug delivery to cancer stem cells (using different nanocarriers such as liposomes, micelles, nanotubes, nanogels) 2-Targeting resistance genes. 3-Destruction of the nest of cancer stem cells (2).

Keywords: Cancer, Nanoparticles, Nanorobot, Nanotechnology, Treatment.

Investigating the effects of Rutin vs. Citalopram on SERT by molecular docking method (Research Paper)

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Introduction: Introduction The transport of serotonin from the synaptic cleft back into the presynaptic neuron is regulated by a protein called SERT, or serotonin reuptake transporter. Dysregulation in SERT function has been associated with depression and anxiety; therefor, this protein stands out as a key target for treating neuropsychiatric disorders, including major depressive disorder (MDD). Selective serotonin reuptake inhibitors (SSRIs), which are commonly used as antidepressants, enhance serotonin activity by inhibiting the SERT. Moreover, one of the frequently prescribed SSRIs is Citalopram. Rutin is a flavonoid glycoside commonly found in various herbs such as Ruta graveolens. This compound exhibits antioxidative and anti-inflammatory properties. Remarkably, Rutin demonstrates the capacity to enhance the strength of blood vessels, as well as capillaries. In this study, we compare the binding affinity of Rutin and Citalopram to SERT by molecular docking method. Analyzing whether Rutin exhibits a more potent bond with SERT than Citalopram, offers opportunities for exploring new therapeutic agents based on Rutin.

Methods: Materials and Methods In this research, first of all, the structure of SERT was downloaded from the Uniprot website, then preparations, such as the addition of charge and hydrogen ions, were executed using Chimera software. The three-dimensional structures of both Rutin and Citalopram were downloaded from the PubChem website. The binding site of the SERT protein was determined using Deepsite. [Center; X: 36.4195, Y: 184.783, Z: 142.7143 and Dimensions (Angstrom); X, Y, Z: 25.00] Eventually, the execution of the molecular docking was performed utilizing AutoDock Vina in PyRx 0.8 to investigate the binding affinity of Rutin vs. Citalopram to SERT.

Results: Results The achieved results from performing the docking process using PyRx software can be summarized as follows. In terms of their binding affinity, lower RMSD bond, and upper RMSD bond, Rutin and Citalopram are individually represented by the presented data. Rutin: Model #1: [-10.6, 0.0, 0.0] Model #2: [-10.5, 2.125, 3.482] Model #3: [-10.2, 1.715, 2.274] Model #4: [-10.1, 2.005, 8.751] Model #5: [-10.0, 2.356, 8.61] Citalopram: Model #1: [-8.7, 0.0, 0.0] Model #2: [-8.7, 0.019, 0.986] Model #3: [-8.6, 1.42, 2.148] Model #4: [-8.1, 3.213, 4.767] Model #5: [-8.0, 3.022, 5.899]

Conclusion: Conclusions According to the results of the molecular docking analysis of Rutin and Citalopram with SERT, it was determined that both compounds revealed negative binding energy. However, Rutin revealed a higher affinity compared to Citalopram. Based on this information, it is indicated that Rutin could potentially help developing innovative therapeutic agents for the treatment of major depressive disorder.

Keywords: Keywords: Rutin, SERT, Citalopram, Molecular docking, Major depressive disorder

Investigating the effects of spirulina plantensis as a functional food (Review)

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Introduction: Spirulina algae is a potential functional food due to its valuable nutritional content, including proteins, essential amino acids, minerals, vitamins, and antioxidant compounds. It is used as a sustainable strategy to prevent protein energy malnutrition in humans and animals. Spirulina is used in many functional foods available on the market, such as yogurt, drinks, pasta, and supplements, alone or in combination with other natural ingredients. This research aims to assess the effects of spirulina algae to determine how well these products work as a source of functional foods.

Methods: Spirulina plantensis, Arthrospira platensis, and functional food were the keywords used in searches for this review study. Since 2017, we have reviewed several databases, including Google Scholar, PubMed, and Scopus. The most pertinent articles were examined after assessing the data's quality and studies were included if they investigated the effects of Spirulina platensis on human health outcomes.

Results: Arthrospira platensis, also known as spirulina, has various properties that make it a potential functional food. It has been found to have potential reducing effects on chronic diseases such as blood pressure, blood lipids, and high blood sugar, and may be useful in preventing metabolic syndrome. It also improves the growth of probiotics, has antimicrobial and

antioxidant activity, reduces inflammation without inhibiting innate immune defenses, and has various other health benefits such as aiding weight gain, treating anemia and malnutrition, preventing muscle atrophy, and promoting muscle regeneration. Spirulina has also been used to enhance the nutritional value of bread and replace artificial additives in the dairy industry. However, caution should be exercised as there are some noticeable side effects such as insomnia, stomach issues, liver toxicity, and autoimmune hepatitis, especially in patients being treated with certain medications.

Conclusion: Spirulina platensis shows promise as a functional food with potential health benefits. However, further research is needed to determine the optimal dose and duration of supplementation and to better understand the mechanisms underlying the observed effects. Spirulina platensis may be a useful dietary supplement for individuals seeking to improve their health, but more research is needed before specific recommendations can be made.

Keywords: Spirulina plantensis, Arthrospira platensis, Functional food, Lipid profile, Glycemic control

Investigating the effects of using blended learning method on medical students (Review)

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Introduction: Blended learning is actually a combination of traditional face-to-face education with modern electronic education methods, which has become an effective method in the education of medical students due to the rapid growth in the use of technologies in teaching and learning. For this method, electronic learning is used to complete academic lessons in conjunction with additional workshops to enhance clinical performance. As Internet infrastructure continues to develop, along with students' access to the Internet, the Internet can now be used to supplement traditional and conventional training methods. The purpose of this review is to investigate the effect of using blended learning method on medical students.

Methods: A review study was conducted in 2023 with the keywords of “Blended learning”, “Blended learning in medical students”, “Medical Education” and their Persian terms in Google Scholar search engine and Pub Med, Web Of Science, SID databases. The applied restrictions include the time limit of 2023-2018, Farsi and English language studies, descriptive, analytical, interventional and qualitative articles. Books, thesis and review articles were excluded. The articles related to the study were also evaluated through a researcher made evaluating tool. Finally, 14 articles were reviewed from the extracted articles, the articles which full text was available.

Results: Based on the studies, the effects of combined learning on students include improving students' learning (4 studies), Participation of learners (1 study), academic progress of students (3 studies), improving thinking and decision-making methods (2 studies), improving the ability to solve problems (3 studies), improving the level of knowledge (3 studies), improving clinical skills (3 studies), improving critical thinking (1 study), improving comprehensive performance in exams (2 studies), facilitating learning and ease of understanding (2 studies), correcting the study method of learners (1

study), increasing students' self-confidence (1 study), improving cognitive ability (1 study), independent and student-centered learning (4 studies), flexible learning time (1 study), improving teacher-student interaction and asking questions more easily (3 studies), Creating interest and motivation in learning (3 studies). Students were in the fields of medicine, dentistry, health, nursing, and master's students in medical sciences.

Conclusion: This study shows that blended learning has many positive effects on the learning of medical sciences students. It is effective in improving medical sciences students' learning and this method has positive effects on improving clinical skills and students' motivation. It is suggested to use this method during lectures and clinical courses.

Keywords: Medical Education, Blended learning, Learning

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Investigating the expression of HMGA-1 and HMGA-2 genes in tumor and normal samples (tumor margin) of gastric cancer in Khuzestan (Research Paper)

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Introduction: Gastric cancer is one of the most common malignancies in the world, which leads to high mortality. HMGA family (High-mobility group) are regulatory proteins of chromatin structure and are particularly important in tumorigenesis. This study aimed to investigate the expression changes of this protein in the affected population of Khuzestan (Iran).

Methods: In this study, a total of 60 tissue samples including 30 gastric cancer tumor samples and 30 non-tumor samples (tumor margins) were purchased from the tumor tissue bank of Imam Khomeini Hospital in Ahvaz. After extracting RNA and evaluating its quantity and quality with a nanodrop device and agarose gel electrophoresis, a Real-time PCR technique was used to check the expression of HMGA-1 and HMGA-2 genes. Statistical analysis was performed using GraphPad Prism 9.2.0.332 statistical software and t-test and ANOVA statistical analysis methods.

Results: The results showed that comparing the relative expression of the HMGA-1 gene in tumor samples to non-tumor samples increased by 17 times and significantly (P-value=0.0001). Also, this increase in HMGA-2 gene expression in tumor samples was 15 times compared to normal samples and showed a significant increase (P-value=0.0038).

Conclusion: The results showed an increase in the expression of HMGA-1 and HMGA-2 genes in cancer cells of the affected population of Khuzestan province (Iran). This issue and the identification of their mechanism can be helpful in the treatment of patients; Therefore, it is recommended to identify the effect path of these genes in future studies.

Keywords: Gastric cancer; HMGA1, HMGA2, clinicopathological features

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Investigating the expression of some genes involved in the survival of Campylobacter jejuni in gastric acid: A bioinformatics exploration (Research Paper)

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Introduction: Campylobacter jejuni is a bacterial pathogen that causes gastroenteritis in humans. The ability to survive stomach acidity is a fundamental requirement for C. jejuni to colonize the host and cause disease. Infection with C. jejuni, which causes diarrhea, is one of the most common causes of Guillain-Barré Syndrome (GBS) is a rare but serious autoimmune disorder that affects the peripheral nervous system. C. jejuni modulates gene expression in response to acid shock in vitro and in vivo, and this response is important for its survival in the stomach. The acid adaptive tolerance response in C. jejuni permits increased survival at lethal pH values, and further research is needed to better understand the transcriptional response of C. jejuni to acidic conditions and its role in the pathogenesis of this bacterium. The acid adaptive tolerance response in C. jejuni permits increased survival at lethal pH values, and further research is needed to better understand the expression of genes in transcriptional response of C. jejuni to acidic conditions and its role in the pathogenesis of this bacterium.

Methods: By utilizing the GSE73793 microarray dataset, we employed a combination of GEO2R online tools and R software to extract and analyze the data. Genes exhibiting significant differential expression, determined by parameters P<0.05 and LogFC>|1|, were identified. Subsequently, we isolated the expression profiles of these relevant genes, focusing on those exhibiting increased expression. To gain further insights, we utilized the STRING database to predict protein networks associated with these genes. The resulting network was visualized using the Gephi software.

Results: Through careful analysis, we discovered a collection of genes (rplB, rpoA, rplE, tuf) that exhibited notable changes in expression, indicating their potential involvement in the survival of C. jejuni in gastric acid conditions.The

(rplB) gene was found to be an one of the primary rNA binding proteins that makes several contacts with the 16S rRNA in the 70S ribosome.The (rpoA) gene, was found to DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. (rplE) is one of the proteins that binds and probably mediates the attachment of the 5S RNA into the large ribosomal subunit, where it forms part of the central protuberance. In the 70S ribosome it contacts protein S13 of the 30S subunit (bridge B1b), connecting the 2 subunits; this bridge is implicated in subunit movement. At the end (tuf) gene is DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. These findings suggest that these genes play important roles in the virulence of C. jejuni and could be potential targets for the development of interventions to prevent and treat infections.

Conclusion: Altogether, this study uncovers the transcriptional profile of C. jejuni in response to acidic conditions as those encountered in the stomach and contributes to a better understanding of the genetic response of C. jejuni to acidic conditions, paving the way for potential therapeutic interventions and control measures to mitigate the impact of this pathogen on human health. In addition, our results demonstrate that acid stress jump-starts C. jejuni for efficient gut colonization and host pathogenesis.

Keywords: Campylobacter jejuni, gastric acid, Gene expression, bioinformatics analysis, R software

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Investigating the Importance and function of Silver Nanoparticles against Staphylococcus Aureus Infections (Review)

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Introduction: One of the most prevalent pathogens in infections, is Staphylococcus aureus. S. aureus is also common in a wide variety of infections, including those that affect the blood, respiratory system, skin, and soft tissues. Chronic and recurrent infections are still caused by major treatment failures. Silver nanoparticles (AgNPs), which are extremely small (1-100 nm) metallic silver particles, are one promising antibacterial agent that is emerging as a new therapeutic option against a variety of infections. This study aimed to investigate the Importance and function of Silver Nanoparticles against Staphylococcus Aureus Infections.

Methods: This study with the title Investigating the Importance and Function of Silver Nanoparticles against Staphylococcus Aureus Infections has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Silver's inhibitory impact is likely the culmination of several different mechanisms of action. Many studies indicate that silver ions interact with proteins' SH groups and are crucial for the inactivation of bacteria. It has been observed that silver ions at micromolar concentrations decouple oxidative phosphorylation, which inhibits respiratory chain enzymes or alters membrane permeability to protons and phosphate, from respiratory electron transport. Scientists treated bacteria like Staphylococcus aureus with AgNO3 to demonstrate the activity of silver ions on both Gram-negative and Gram-positive bacteria. They then examined the impact on cell morphology using combined electron microscopy (TEM and SEM) and X-ray microanalyses. Similar morphological changes in E. coli and S. aureus were observed after exposure to silver ions, including the separation of the cytoplasm membrane from the cell walls and the appearance of an electron-light region in the centre of the cells. This region contained condensed DNA molecules and was likely formed to shield DNA from damage caused by the silver ions. There were also tiny, electron-dense granules that were either deposited inside the cells or around the cell wall. The observed alterations in morphology are supported by the published findings. and that bacteria enter an active but uncultivable stage and eventually perish in the presence of silver ions. Also, given that they discovered that silver ion solution had higher inhibitory activity against E.

coli than against S. aureus, they hypothesized that the thickness of the peptidoglycan layer of gram-positive bacteria may partially impede the action of the silver ions.

Conclusion: The current study demonstrates that AgNPs are a unique treatment agent against extracellular and intracellular bacteria. AgNPs were shown to be very potent in eliminating extracellular bacteria with low toxicity towards human cells. AgNPs also exhibited improved antibacterial activity in combination with antibiotics against extracellular bacteria. The results showAgNPs against extracellular bacteria. This is important since some bacteria, such as S. aureus, have the ability to persist intracellularly and may lead to difficult-to-treat chronic and recurrent infections.

Keywords: Silver Nanoparticles, Staphylococcus Aureus, Infections

Investigating the influencing factors on the tendency to self-medication of traumatized elderly: a case study of Shiraz elderly (Research Paper)

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Introduction: The fifth cause of death in patients over 65 years old is trauma, and 28% of people who die from trauma are elderly, while only 12% of trauma patients are elderly. Trauma is the most common cause of injury among the elderly. In this research, the aim of the comparative study of the tendency to self-medication among the traumatized elderly in Shiraz city was based on the factors of residence, gender, trust and lack of trust in city doctors, literacy and whether or not they have insurance.

Methods: In this research, to obtain information, a researcher-made questionnaire was used, in which questions related to independent and dependent variables were asked, and to analyze the data, average comparison statistics and one-way analysis of variance were used.

Results: Overall, the findings of the research showed that there is less self-medication among elderly men with trauma than elderly women, and those who have insurance coverage commit less self-medication than those who are not covered by insurance. Those who have more trust in city doctors and were literate and also from urban areas tend to self-medicate less among them. On the other hand, the elderly who had less trust in doctors, are illiterate and are from rural areas, tend to self-medicate more among them.

Conclusion: Elderly people should take measures to reduce self-medication along with doctors and the government as three sides of a triangle. In the first stage, the elderly (especially women and rural elderly) should be fully aware that with uninformed self-treatment, not only the disease caused by their trauma will not be relieved, but it will also bring bad consequences. In the second stage, doctors should raise The capacity of self-compassionate acceptance of the elderly, especially the elderly with trauma, and in the third

stage, the government should help the elderly with coherent and efficient policies, including insurance coverage for the elderly.

Keywords: Elderly, trauma, self-medication

Investigating the inhibitory effect of the fractions of extracellular secretions (Postbiotic) in Pediococcus probiotic bacteria on Gastrointestinal cancer (Research Paper)

Reyhaneh Heshmati,[1] Sepideh Khaleghi,[2] Ebrahim Kargar,[3] Masoud Javanmardi,[4,*]

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Introduction: As per the 2020 report by the World Health Organization, cancer is the second most prevalent cause of death worldwide, causing almost 10 million deaths annually. Colorectal cancer accounts for a significant portion of the statistics, with approximately 2 million cases and 1 million fatalities. Nowadays a variety of studies have indicated that microorganisms function in the gastrointestinal have a vital role in the regulation of human homeostasis and the immune system. Therefore, microbiome manipulation and general metabolism of intestinal microflora are effective strategies for cancer treatment which includes probiotics and postbiotics. While probiotics are beneficial, postbiotics are considered to be a safer option with fewer side effects. Regarding postbiotics potential effectiveness of health as a promising and emerging method for cancer prevention and treatment, it is crucial to investigate the postbiotics as an anticancer.

Methods: The present study was employed postbiotic, derived from bacterial strains, to explore their inhibitory and anticancer effects on colon cancer cells. First of all, the strains of Pediococcus was isolated in the laboratory. Then, the cell-free supernatant (CFS) known as postbiotic was extracted, and provided through the lyophilization method. The cytotoxicity effect of the postbiotic sample was tested on the HCT-116 colon cancer cell line. The sample of postbiotic was prepared at concentrations of 50, 100, 250, 500, and 750 (nM), followed by MTT assay at 24, 48, and 72-hour intervals, and calculated IC50. The flow-cytometry was arranged by postbiotic concentration at 750 nM over a period of 48 hours to examine Apoptosis and Necrosis clles and the cell cycle arrest and ROS was analysed.

Results: The anticancer properties of postbiotic were studied based on the preparation of isolated strains. The determination of statistical significance was made with Two-way ANOVA. The MTT assay findings have clarified that postbiotic can able to induce cytotoxicity in HCT-116 cells, depending on

concentration and time. There is a significant difference in the evaluated results of postbiotic with a concentration of 750 nM. The reduced cell survival result after 72 hours for cell-free supernatant of Pediococcus (CFSP) was obtained as 67%. According to the results, treatment of cancer cell lines with determined IC50 increased the percentage of cells in early and late apoptosis phases compared with the negative control. The percentage of induced apoptosis (early apoptosis) was 8.64%. In comparison to the untreated control cells, treatment with CFSP at a concentration of 750 µg/ml for 48 hours led to an increase in the Sub-G1 phase of cells. CFSP treatment was associated with the highest sub-G1 phase of 62.61% when compared to the negative control. The analysis of results reveals that the postbiotic possess notable anti-cancer properties.

Conclusion: The findings demonstrated that the lab-made postbiotic, the cell-free supernatant, might have inhibitory and lethal effects on colon cancer. It will be necessary to carry out further examinations and investigations to get more definitive results.

Keywords: Probiotic; postbiotic; cell-free supernatant; colorectal cancer; anticancer therapy.

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Investigating the interaction and expression level of YWHAE mRNA and lncRNA CCAT1 in AML cancer (Research Paper)

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Introduction: Introduction: A kind of blood cancer that targets the bone marrow and blood cells is known as acute myeloid leukemia (AML), also referred to as acute myelogenous leukemia. The disease signs and symptoms include weariness, infections, and bleeding issues. In recent years, the vital role of long non-coding RNAs (lncRNAs) in tumor formation and progression has been widely investigated. One of the most important LncRNAs known to be associated with tumor development is CCAT1. Considering the importance of the multifunctional protein YWHAE in signal transduction, cell cycle regulation, and apoptosis, the purpose of this study is to investigate the interaction and expression level of YWHAE mRNA and lncRNA CCAT1 in AML cancer, based on the bioinformatic studies.

Methods: Methods: In order to check the expression change of YWHAE and CCAT1 genes, in acute myeloid leukemia, we used the GEO website (Gene Expression Omnibus). By mRNA expression datasets in this site, we analyzed the differentially expressed genes (DEGs) related to AML cancer. In the next step to confirm the data, we used Gene Expression Profiling Interactive Analysis (GEPIA) and previous researches. After data validation, Web Server LncRRIsearch was used to investigate the interaction of YWHAE mRNA and lncRNA CCAT1. For further analysis, we obtained the 3D structure of YWHAE protein (from the PDB website https://www.rcsb.org/) and we prepared YWHAE protein for AutoDock and obtained the 3D structure of lncRNA (using 3D RNA/DNA webserver http://biophy.hust.edu.cn/new/). Finally, we showed the interaction between CCAT1 LNCRNA and YWHAE protein by discovery.

Results: Results: Data from the GEO website analysis revealed that CCAT1 was up-regulated gene and YWHAE was downregulated gene in AML cancer. For the YWHAE protein, in the GEPIA database, 173 patient samples and 70 healthy samples were investigated, and based on the produced box plot

diagram, we saw that the expression of the YWHAE protein was reduced in this cancer. Our research revealed that the energy binding of YWHAE mRNA and lncRNA CCAT1 is -16.36 Kcal/mol. Finally, analyzing the docking showed YWHAE protein is capable to interact with lncRNA CCAT1 too.

Conclusion: Conclusion: Our results showed that YWHAE mRNA interacts with CCAT1 LncRNA, and this can be the reason for the decrease in YWHAE expression.

Keywords: Keywords: LncRNA, AML, Cancer, CCAT1, YWHAE

Investigating the knowledge level of palliative care in the elderly with chronic diseases living in Shiraz city (Research Paper)

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Introduction: Determining the level of knowledge of the elderly about palliative care and identifying their needs can play an important role in encouraging the use of palliative care services. The development of educational resources related to palliative care for the elderly requires a lot of information about the level of knowledge exists in this group, so this study was conducted with the aim of determining the knowledge level of palliative care in the elderly with chronic diseases living in Shiraz city.

Methods: In this cross-sectional study, 200 elderly people with chronic diseases in Shiraz city were selected using available sampling. The data collection tool was demographic factors questionnaire and PaCKS palliative care knowledge scale questionnaire. Data analysis was done using SPSS version 26.

Results: 51% of the study participants were over 75 years old and the chronic disease of most of the elderly (44%) was cardiac. 40% of the elderly got their information related to palliative care from the medical staff and 36% of them did not have any source to get information related to palliative care. The mean score of palliative care knowledge was 9.89±3.07, which was evaluated at the average level. 56.5% of the elderly had moderate and poor knowledge about palliative care. The chi-square test showed a significant relationship between the variables of the source of information related to palliative care and the economic status of the samples with their level of knowledge p<0/05.

Conclusion: Considering the level of knowledge of the elderly regarding palliative care, it is suggested to hold training courses in order to maintain and improve the knowledge level of this group. The development of educational

programs by the medical staff in the field of palliative care can play an effective role in improving the knowledge of the elderly.

Keywords: Palliative care, knowledge, elderly, chronic disease

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Investigating the level of EGR1 gene expression in the peripheral blood of Iranian patients with paranoid personality disorder and its relationship with patients' neuromarkers, a brain imaging genetic study (Research Paper)

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Introduction: Currently, there are no definitive proven causes for personality disorders. But there are several possible causes and risk factors that vary by type of disorder, person, and circumstances, and genetic research to understand why personality disorders develop is severely lacking. The aim of this research was to investigate the level of EGR1 gene expression in the blood of patients with paranoid personality disorder and its relationship with the patients' neuromarkers. In this research, 100 patients with paranoid personality disorder and 100 healthy individuals were selected, and the Wechsler test was used to confirm the normal intelligence of the participants, and the EEG test was used to record the electrical activity of the brain, and brain imaging techniques were used. After taking blood from people and transferring to the laboratory, RNA was extracted and Quantitative Real-Time PCR was performed. SPSS.20 was used for statistical analysis. The finding of the research was the correlation between the results of gene expression and the frequency of brain waves of patients with paranoid personality disorder, statistical correlations between the frequency of brain waves and the results of gene expression in patients with paranoid personality disorder. The results of ERG1 evaluation showed a significant and direct relationship between the decrease in beta wave frequency and the decrease in gene expression. The results of relative average gene expression calculated by Livak method for patients with paranoid personality disorder show a decrease in EGR1 gene expression in the group of patients compared to healthy individuals.

Methods: In the current research, the writer was faced with quantitative and qualitative data (two-mode and multi-mode) and the following statistical tests were used to analyze the data in SPSS.20 software in the following order: 1) Checking the normal distribution of data with the Kolmogorov-Smirnov test. 2) Examining the difference in gene expression between healthy and diseased

groups with the mean test of two independent samples. 3) Investigating the correlation of genetic and psychological data with Pearson's correlation test. In this research, patients with paranoid personality disorder among the clients of psychiatric clinics were included in the study after being diagnosed by a psychiatrist based on the diagnostic criteria of the DSM5 book, healthy people were included in the study after a visit by a psychiatrist or clinical psychologist and confirmation of mental health. After selecting the samples of sick people and healthy people with the same physical conditions (including the same age, gender, level of education and social class), people who had one or more criteria of the research output criteria were excluded from the research. Patients were selected from psychiatric clinics in Tehran, Alborz and Isfahan provinces. Finally, 100 healthy samples and 100 patients with paranoid personality disorder were selected and included in the study. After explaining the steps and objectives of the research to the participants, written consent was obtained from them before the beginning of the research. The output criteria of this research are as follows: 1) Healthy and sick samples should not have a history of drug or stimulant abuse or high alcohol consumption at any stage of life. 2) Healthy and sick samples should not have mental retardation. The natural intelligence of people was confirmed by evaluating the Wechsler intelligence test. 3) Healthy samples must have general mental health, which was confirmed by conducting an unstructured psychiatric interview by a psychiatrist. 4) In order to minimize the effect of intervening variables, the selected sick and healthy samples must be free of any other physical or mental illness. 5) In case of a certain important emotional or physical incident up to four months before the sampling, due to the potential effect on the gene expression level, the person in question was removed from the research.

Results: This was despite the fact that there was no significant difference in the expression of this gene in people living in three different cities that were investigated ($p>0.05$). Also, based on the frequency of brain waves obtained by the EEG method in patients with paranoid personality disorder, it was found that there is a significant relationship between the decrease in beta wave frequency and the decrease in EGR1 gene expression. Matsumoto et al. (2012) observed in their study that social separation stress leads to a decrease in EGR1 expression in mice. This decrease in expression was observed in the nucleus of neurons in the cortical part of the brain. The stress applied to these mice had no effect on the expression of EGR1 in the striatum or the expression of other EGR family members. The result of the present research showed that EGR1 gene expression was decreased in people with paranoid personality disorder compared to healthy people.

Conclusion: The present research has investigated the expression of EGR1 gene in patients with this little-known disease with the aim of finding potential biomarkers in paranoid disorder. Such research can help to better understand the mechanisms involved in the occurrence of these diseases. In this study, 100 people with paranoid personality disorder and 100 healthy people were examined as a control group. The obtained results showed that the expression of EGR1 gene in people with paranoid personality disorder has decreased compared to healthy people. By comparing the level of EGR1 gene expression in two groups of healthy and paranoid personality disorder, a statistically significant difference was observed (p=0.001).

Keywords: gene expression, EGR1, paranoid, Wechsler test, brain imaging

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Investigating the Neurodevelopmental and Neurodegenerative Pathology of Down syndrome to Identify Neurophysiological Biomarkers in Patients with Alzheimer's disease: a Narrative Review Study (Review)

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Introduction: The human brain is a complex organ composed of well-organized parts that work together to control body functions and regulate the higher functions of the mind that make us human. The growth of the human brain begins as a neural groove from a specific part of the ectoderm, the neuroectoderm, and forms the neural tube after the end of the third week of pregnancy. Primary and secondary brain vesicles through the progressive production of neural tissue from the neural tube around 4 and 5 weeks of gestation, respectively. The ventricles of the brain produce cerebrospinal fluid, which regulates the homeostasis of the interstitial fluid of the brain and acts as a hydromechanical protector of the central nervous system. People with Down syndrome (DS) suffer from developmental delay, mental retardation, and early onset of neurodegeneration, Alzheimer-like disease, or early-onset dementia caused by an extra chromosome 21. Studying the changes at the anatomical, cellular, and molecular levels involved may help to understand the pathogenesis and develop targeted therapies, not only medical, but also surgical, cell therapy, and gene therapy, etc., for people with DS. Cross-frequency coupling (CFC) mechanisms play a central role in brain activity. The pathophysiological mechanisms underlying many brain disorders, such as Alzheimer's disease (AD), may produce unique patterns of brain activity detectable by electroencephalography (EEG). Identifying biomarkers for the diagnosis of AD is also an ambition among research teams working in Down syndrome (DS), given the increased susceptibility of individuals with DS to develop early-onset AD (DS-AD). We aim to identify key developmental manifestations. Neuroscience, finding knowledge gaps, and trying to build molecular networks to better understand mechanisms and clinical significance.

Methods: This study is a descriptive study with a Narrative Review approach in 2023 by searching for keywords such as: Neurodevelopmental, Neurodegenerative, Pathology, Neurophysiological, Biomarkers Alzheimer in reliable databases such as: Scopus, Elsevier, PubMed , Web of Science was done. Finally, 15 articles were found, of which 10 were included in the study.

Results: According to the studies from the articles, the results obtained are that, theta-gamma phase amplitude coupling (PAC) may be one of the first signs of EEG AD, and therefore may be used as an auxiliary tool for the diagnosis of cognitive decline in DS-AD works. We suggest that this field of research could potentially provide clues to the biophysical mechanisms underlying cognitive dysfunction in DS-AD and create opportunities to identify EEG-based biomarkers with diagnostic and prognostic utility in DS-AD. Despite growing preclinical and clinical evidence supporting the use of EEG to investigate the effects of AD pathology on neurophysiological parameters, currently applied diagnostic criteria still do not support the use of EEG-based biomarkers in AD clinical practice. A similar scenario has been observed in the field of research aimed at identifying biomarkers for AD in DS. For example, the protocol of the most ambitious AD biomarker initiative to date in adults with DS, the Alzheimer's Down Syndrome Consortium Biomarker Syndrome (ABC-DS), includes advanced measures of MRI but not EEG as outcome measures of functional connectivity. In this perspective, we rationalize the pursuit of PAC as a potential auxiliary tool in the study of pathophysiological processes underlying brain dynamics in DS-AD, as well as in the identification of EEG-based biomarkers with potential diagnostic and prognostic tools in DS-AD. From a basic science perspective, continued investigation of neural network dynamics in mouse models of DS may help to increase our understanding of how AD pathology evolves in individuals with DS, as well as to expand knowledge of the early neurophysiological symptoms of DS-AD. It could potentially be of clinical use. From the perspective of clinical practice, the development of non-invasive, low-cost and easily accessible biomarkers (such as EEG-based ones) for the diagnosis of AD may be an important step towards identifying individuals in the pre-clinical or pre-dromal stage. This disease, especially in the most susceptible populations as the case of DS.

Conclusion: Understanding the changes and developing characteristics of Down syndrome will help target therapy to improve clinical outcomes. Early targeted intervention/treatment for DS-related manifestations in the prenatal or postnatal period may be beneficial to rescue neuropathology and neurodegeneration in DS.

Keywords: Neurodevelopmental, Neurodegenerative, Pathology, Neurophysiological, Alzheimer Biomarkers

Investigating the potentials of paying attention to the gut-testicular pathway in the treatment of male infertility: a review study (Review)

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Introduction: In the quest to understand male fertility, an intriguing player has emerged from the shadows – the gut microbiome. Recent studies have illuminated the profound impact of our gut's microbial residents on the intricate web of factors that govern sperm health and reproduction. This article delves into the intricate relationship between the gut microbiome and male fertility, highlighting how the gut's delicate balance can sway the scales of spermatogenesis and reproductive succes In the following, we will describe some roles of the gut microbiome that have been mentioned in recent studies.Sperm Health: At the heart of this connection is the intriguing possibility that the gut microbiome plays a pivotal role in shaping the health of sperm. It has been revealed that the composition of gut microbiota can influence essential elements like testosterone levels and sperm production.Normal Spermatogenesis: The journey to healthy sperm is not without its challenges, and the gut microbiome is sensitive to dietary and environmental influences. A high-fat diet, for instance, can disrupt the harmonious process of spermatogenesis and impede sperm motility.Gut-Testis Axis: Enter the gut-testis axis, a complex interplay between the gut, the immune system, and the reproductive system. It's becoming increasingly clear that the gut microbiome contributes significantly to male reproduction by providing vital nutrition, immunity, and signaling support. This microbial ecosystem may even play a role in guiding spermatogonial stem cells on their transformative journey to becoming fully-fledged sperm.Probiotics and Prebiotics: Armed with this knowledge, researchers are exploring novel therapeutic avenues. Probiotics, prebiotics, and even fecal microbiota transplantation have emerged as potential tools in the battle against male infertility. Prebiotics, for instance, hold the power to boost specific beneficial microbes like Bifidobacterium and Lactobacillus, and intriguingly, have shown promise in accelerating sexual maturity in experimental models.In this article, we embark on a fascinating journey through the crossroads of the gut and male fertility, unraveling the intricate ways in which our gut microbiome can shape the path to fatherhood.

Methods: The method of this study was to review the articles available in ISI Schopus, PubMed and Google Scholar.

Results: The gut microbiome plays a crucial role in normal spermatogenesis and can be negatively impacted by diet and environmental factors. Prebiotics can increase levels of certain probiotics, such as Bifidobacterium and Lactobacillus, as well as accelerate sexual maturity in rats. The gut microbiota supports male reproduction via nutrition, immunity, and signaling, and can promote spermatogonial stem cells differentiation into sperms. Calcium plays a decisive role in the fertilization process and improves sperm motility and sperm capacitation. Impairment of spermatogenesis and sperm motility can be caused by high-fat diet-induced dysbiosis of gut microbes. Therapeutic options such as probiotics, prebiotics, and fecal microbiota transplantation are potential treatments for male infertility.

Conclusion: Therefore, prebiotics can play a role in the spermatogenesis axis by increasing levels of certain probiotics and accelerating sexual maturity in rats. The gut microbiota also supports male reproduction via nutrition, immunity, and signaling, and can promote spermatogonial stem cells differentiation into sperms. Calcium also plays a crucial role in the fertilization process and improves sperm motility and sperm capacitation. However, further research is needed to fully understand the role of prebiotics in the spermatogenesis axis.

Keywords: Male fertility, microbiome, gut-testicular axis

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Investigating the Prevalence of Antibiotic Prophylaxis in Elderly Women With Urinary Tract Infection (Research Paper)

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Introduction: Introduction: Urinary tract infection is one of the most common infectious diseases in women. This research was conducted with the aim of determining the pattern of antibiotic resistance in micro-organisms that cause office infection and the effect of common antibiotics in treating the disease in elderly women

Methods: Methods: The current study is a cross-sectional study. The sampling method was a census and the target population included all female patients over 65 years of age with urinary tract infections who were admitted to the infectious and urology departments of Shahid Mostafa Khomeini Hospital, Tehran, Iran from April 2017 to March 2022 and received antibiotics during the treatment period. have done, a study was conducted on 150 elderly female patients aged 65 and over with urinary tract infection. After culture and final confirmation of infection, urine samples were analyzed for microbial sensitivity by standard disc diffusion method. The relationship between the infecting strain, the results of the antibiogram culture, and the demographic factors of age, underlying disease, and length of treatment were investigated.

Results: Results: Escherichia coli was diagnosed as the dominant strain in 120 patients. 11 types of antibiotics were identified in the antibogram culture, all patients (100%) were sensitive to Amikacin. The most resistant antibiotic was Cefalotin, which 83% of patients showed resistance to. The infecting strain and antibiogram culture results had no significant relationship with the demographic factors of age, underlying disease, and length of treatment ($P>0.05$).

Conclusion: Conclusion: The results of the study showed that the most resistant and sensitive antibiotics examined in the study were Cefalotin and Amikacin. Due to the high prevalence of urinary tract infection in the elderly, its correct diagnosis

Keywords: Keywords: Urinary infection Antibiotic resistance Elderly Underlying disease

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Investigating the prevalence of coinfection pulmonary fungal in patients with pulmonary tuberculosis: A systematic review (Review)

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Introduction: Tuberculosis (TB) is one of the most important causes of respiratory diseases. they illustrate that Pulmonary tuberculosis (PMT) is associated with opportunistic pulmonary fungal (PF) infections, which cause significant mortality worldwide. In this study, we investigate the prevalence of coinfection pulmonary fungal in patients with pulmonary tuberculosis.

Methods: This is a descriptive-analytical review study that, in addition to using online English articles published in Google Scholar, Science Direct, and PubMed databases, as well as Persian Sid, Magiran, and Cilivica in the period of 2018-2023 was reviewed, but our selection criteria were mostly Persian databases. The keywords were used coinfection, pulmonary tuberculosis, and pulmonary fungal infections.

Results: According to the study conducted in a certain period of time, the synergy of PMT infection with pulmonary fungal has been greatly expanded since 2018 and led to the occurrence of acute symptoms in patients, but this synergy in the previous years of 2018 was Sporadic. The main factors associated with the coinfection development of PMT and PF infections, which can be mentioned are the Immunodeficiency of people, underlying diseases, the use of broad-spectrum antibiotics, the geographical region, and even the disorder in the structure of the lung. Studies have proof that the family of opportunistic fungi such as Aspergillus and Candida are most involved in lung infections, and Aspergillus fumigatus, Aspergillus flavus, Candida albicans, and Aspergillus niger positive influence respectively.

Conclusion: In Pulmonary Tuberculosis, it has been manifest that pulmonary fungal infections are highly common. The most common coinfections are opportunistic fungal species such as Candida and Aspergillus. It causes tissue and systemic damage following the synergism of Fungal pneumonia infections and TB .

Keywords: coinfection , pulmonary tuberculosis , and pulmonary fungal infections

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Investigating the relationship between marital quality of life and family health: a descriptive review study (Research Paper)

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1.
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Introduction: Marital quality is a multidimensional concept that includes positive experiences such as feelings of love, care and satisfaction in the relationship. In some studies, the quality of married life has been mentioned as the most important indicator of family health. The purpose of this study is to investigate the relationship between the quality of married life and family health in a narrative review

Methods: This study in 2022 with steps, study question design, search, which in Google scholar search engine and databases such as SID, PubMed, Science Direct, Scopus, with keywords such as "couple", "importance", "quality of married life", "parenting style" "Physical health" and "quality of sexual life" were performed. Then, related studies were identified from the period of 2005 to 2022, and studies were selected (after screening the title, abstract and full text with the help of strob checklist). Among the 43 studies, 13 studies were selected to announce the results.

Results: According to what is mentioned in 13 articles, the quality of married life has a direct and two-way relationship with the physical and sexual health of the couple. So that in 3 studies, people with good quality of married life had good physical health, and in 4 studies, the quality of sexual life of people was related to the quality of their married life, and people with high quality of married life reported a higher quality of sexual life. In 3 studies, people with a higher quality of married life had less stress, anxiety and depression, and the general health score was reported to be higher in one of Yera Ifred's studies with a higher quality of married life. 6The study pointed to the relationship between desirable quality of married life and social factors. People with high quality of married life were more regularly present in the work environment. Also, 3 articles pointed to the quality of married life and the choice of reasonable parenting styles. It should be mentioned that some studies overlapped with each other.

Conclusion: What is obtained from the study shows the great importance of the quality of married life in different dimensions of health in people's lives. In this way, with the knowledge that the quality of married life of couples affects

all dimensions of health, it is hoped that programs to strengthen this matter will be prepared and formulated by health professionals.

Keywords: Family health, quality of married life, couples

Investigating the relationship between microdeletions of the AZF region in men and recurrent miscarriage in their wives in the Iranian population (Research Paper)

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Introduction: Microdeletions in the AZF regions located in the male chromosome can be a possible factor affecting the occurrence of recurrent miscarriage. The aim of this study is to investigate the presence of deletions in the AZFa, AZFb and AZFc regions in men's chromosomes and its relationship with recurrent miscarriages in their wives in the Iranian population.

Methods: In this case-control study, 120 healthy (neurospermic) men with a history of two or more consecutive abortions in their wives and also 120 healthy men without a history of repeated abortions in their wives with at least one healthy child were studied as a control group. After sampling and extracting DNA from people's blood, microdeletions of AZF region were evaluated by Multiplex PCR method. After examining the PCR product on Agarose gel, the results were analyzed with SPSS software (version 20).

Results: There was no deletion in any of the 120 people in the control group. In 120 men whose wives had at least 2 abortions and at most 3 consecutive abortions, there were 40 deletions, including 20 deletions in the sY134 (AZFb) region and 10 deletion in each of the sY127 (AZFb) and sY254 (AZFc). The analysis of the statistical results showed that occurrence of microdeletions in the sY134 (AZFb) region has a significant relationship with the occurrence of abortion (p-value: 0.03).

Conclusion: Men with AZFb usually stop developing sperm (that is, they have no sperm-producing cells), which can sometimes be completed with medication. Therefore, the value of genetic examination is determined from

here, which genetic position candidates for assisted reproductive methods are in, and what the outcome of these measures should be predicted. On the other hand, examining and reflecting on the results reported in various articles as well as the present study highlights the fact that there is a possibility of a significant relationship between microdeletions of AZF regions in men and repeated abortions in their wives. However, it is suggested to conduct a more extensive study on a large statistical population with a larger sample size to make a more definitive decision.

Keywords: Recurrent Abortion, Microdeletions of AZF region, Multiplex PCR

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Investigating the relationship between Trait Emotional Intelligence and level of Empathy in schizophrenic patients referred to Rasoul Akram Psychiatry Clinic. (Research Paper)

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Introduction: Schizophrenia is a clinical syndrome consisting of a variable but profoundly destructive psychopathology that involves Cognitive, Emotion, Perception and other aspects of behavior, and no social class is immune to it. One of the main indicators for Schizophrenia is social disability that includes social skills, interpersonal relationships, and self-care. Considering the importance of this field; in recent years researchers has paid attention to uncover wider areas of emotional and social problems of people with Schizophrenia. One of these areas is the investigation of the emotional intelligence in schizophrenic patients. Compared to normal individuals, people with schizophrenia have defects in different dimensions of emotional intelligence. Another characteristic of schizophrenic patients that has attracted the attention of researchers, is violent behavior. In fact, it has been determined that there is an important relationship between schizophrenia and violence. It has been found that the main cause of violent behavior among schizophrenic patients is their difficulty in empathizing with others. However, the main cause of lack of empathy in schizophrenic patients is not clear. For this reason, the purpose of this research is to investigate the relationship between emotional intelligence of schizophrenic patients and their level of empathy.

Methods: In this research, available sampling method was used and ninety patients referred to the clinic with a definite diagnosis of schizophrenia were asked to answer the Trait Emotional Intelligence Questionnaire (TEIQue-SF) and Toronto Empathy Questionnaire (TEQ). After collecting the data, the statistical method of multiple regression analysis was used to analyze the data.

Results: According to regression analysis, the results showed that there is a relationship between trait emotional intelligence and level of sympathy, and this relationship was observed in different dimensions of trait emotional intelligence with level of sympathy.

Conclusion: More emotional intelligence leads to more empathy. In fact, emotional intelligence strengthens empathy. Therefore, by using psychotherapy techniques to increase emotional intelligence, it is possible to reduce many behavioral problems of schizophrenic patients.

Keywords: Schizophrenia, Traits Emotional Intelligence, Empathy

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Investigating the replacement of postbiotics in people sensitive to probiotics: a systematic review (Review)

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Introduction: The use of probiotics has become popular in recent years for the treatment of digestive diseases. However, there are reports of sensitization in certain groups of people. Postbiotics are the metabolic side products of probiotics, which have been considered as an alternative to probiotics in these people. This systematic review was conducted with the aim of evaluating the effect of postbiotics in people sensitive to probiotics.

Methods: The keywords "Probiotics", "Postbiotics", "Probiotics sensitivity" and "Digestive diseases" were used in a comprehensive search of databases such as PubMed, Scopus, Web of Science, Google Scholar and Science Direct to find studies aimed at investigating the effect of postbiotics. It was done in people sensitive to probiotics. During this research, the studies that met our desired criteria were analyzed.

Results: In total, among the 77 articles resulting from the search, finally 25 articles were included in the study based on matching the input and output criteria for data extraction. Based on the data obtained, post-biotics are effective in reducing the symptoms of people sensitive to probiotics, including bloating, gas and diarrhea. However, evidence for their effectiveness in other gastrointestinal symptoms was limited. This study also showed that the use of different concentrations of postbiotics have different effects on gastrointestinal symptoms.

Conclusion: The results of this study show that postbiotics may be a potential alternative to probiotics in people sensitive to probiotics. However, more studies, including case-control studies and group studies, are needed to determine the types of postbiotics and their optimal concentrations to investigate these special conditions. In addition, it is necessary for specialists in this field to consider the individual characteristics of the patient when prescribing postbiotics to reduce gastrointestinal symptoms in people sensitive to probiotics.

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Keywords: probiotic, postbiotic, probiotic sensitivity, gastrointestinal diseases

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Investigating the risk factors and clinical characteristics and pathology of colorectal cancer in the population of Fars province (Research Paper)

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Introduction: One of the most important types of cancer in the world is colorectal cancer (CRC), which has become a major health problem and is considered the cause of death in the world. Colorectal cancer is the third most common cancer in men and the second most common cancer in women in our country. Colorectal cancer is divided into two categories: hereditary and sporadic. Hereditary colorectal cancers account for 5 to 10% of colorectal cancers, while the rest are isolated colorectal cancers that occur due to somatic mutations in colon and rectal cells. Single-cell CRC occurs in old age and its maximum incidence is after the age of 50. Colorectal cancer is one of the most common malignant tumors, the prevalence of which is increasing in our country. Among the risk factors of this disease, gender and age can be mentioned as important risk factors for colon cancer, so that, for example, women have more survival and less risk of dying from colon and rectal cancer than men. Regarding age, although the probability of colorectal cancer in middle-aged people is 5%, but 90% of people who have this cancer are more than 50 years old. A study in 1992 in Fars province showed that, with the exception of rectal cancer, the standard annual incidence rates cut off from the age of 25 (TAASIR) for other cancers examined in men were almost twice that of women, and this difference was statistically significant in the case of colon = 0.056. (P The purpose of this study is to investigate the prevalence of risk factors and prognostic factors of colon cancer in these patients for proper planning to determine risk factors to control and prevent this cancer, because the severity and importance of risk factors and predisposing behaviors are different in each region and it is necessary to investigate these factors in each region. Risk and prognosis factors in this study include age, gender of

patients, tumor size at the time of diagnosis, tumor grade, tumor stage, degree of invasion and tumor location.

Methods: The present study is a descriptive-cross-sectional study in which the information of 150 men and women with colon cancer confirmed by questioning and file review in Shiraz Medical Sciences Hospitals were selected in 1400 and were evaluated, examined and questioned in terms of non-modifiable factors (age and gender), clinical pathology, tumor characteristics, and the stages and proven prognosis of colon cancer by doctors and experienced people. The resulting data will be analyzed using SPSS version 16 software and frequency indices and chi-square test.

Results: In the present study, this disease was seen in men and women relatively equally. The highest risk factors in CRC are age over 50 years, percentage of involvement of Rectum and Cecum, type of adenoma tumor, tumor size 2-5 cm, histopathology of well-differentiated tissue and most patients in cancer stages (TNM) T in stage 3, N in stage 0 and M in stage 2.

Conclusion: Determining the impact of colon cancer risk factors and prognosis in any population for prevention can play an important role in reducing the incidence of this disease. If it is recommended to carry out more extensive studies considering the risk factors affecting colon cancer and the importance of doing digestive tests such as colonoscopy, blood tests in stool and test of colon cancer markers such as CA 125, CEA CA19-9.

Keywords: Risk factor, colon cancer, metastasis, grade, stage

Investigating the role of EMT-inducing signals in gliomas (Review)

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Introduction: The most frequent malignancy in women and the primary cause of cancer-related deaths globally is breast cancer (BC). Although there have been substantial improvements in clinical therapy, mortality has continued to rise due to the prevalence of breast cancer. Originally, it was believed that long non-coding RNAs (lncRNAs) were just the genome's background noise of transcripts and had no biological purpose. The purpose of lncRNAs has recently come under increased scrutiny. By controlling gene transcription and post-transcriptional processing, studies increasingly demonstrate that lncRNAs have a role in a variety of cellular physiological processes, including proliferation, differentiation, migration, and death. This research looked into how lncRNAs regulate epigenetic changes in breast cancer.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Epigenetic regulation does not alter the DNA sequence to cause heritable changes in gene expression, including DNA methylation, histone modification, genome imprinting, and random chromosome inactivation. Some important functions of lncRNAs are related to the epigenetic control of specific target genes For example, lncRNAs basal-like breast cancer-associated transcript (BLAT1), BCLIN25, and H91 can regulate DNA methylation to participate in tumorigenesis.9) Han found that BLAT1 expression is regulated at the epigenetic level by decreasing DNA methylation of CpG islands in the promoter. Patients with BLAT1-hypomethylated tumors have lower overall survival (OS). The increased BLAT1 expression with hypomethylation at CpG sites may contribute to the aggressive phenotype of breast cancer.57 BCLIN25 increases ERBB2 expression by enhancing CpG methylation of the miR-125b promoter, leading to the downregulation of miR-125b and promoting the occurrence of breast cancer. Also, the lncRNA 91H of the H19/IGF2 locus is transcribed in the H19 antisense orientation. In breast cancer, 91H lncRNA prevents DNA methylation of the maternal allele at the H19/IGF2 locus, thereby increasing the aggressive phenotype of breast cancer cells. In addition, lncRNA also inhibits gene transcription by recruiting histone modification or chromatin remodelling proteins.4 lncRNA HOX

transcript antisense RNA (HOTAIR) plays a critical role in chromatin dynamics through the interaction with histone modifiers resulting in transcriptional gene silencing.59 HOTAIR is participated in the silencing of miR-205 by breaking the balance of histone modification between histone H3 at lysine 4 methylation (H3K4me3) and H3K27me3 on the miR-205 promoter to regulate cyclin J (CCNJ) expression.

Conclusion: Breast tumour formation, diagnosis, and treatment, as well as patient prognosis, are all significantly influenced by lncRNAs. A few lncRNAs have currently had their function mechanisms thoroughly examined in exploratory study. Most lncRNAs' underlying functional mechanisms in breast cancer are still poorly understood, though. The secondary structure of lncRNAs is more complex than that of mRNA, and it has been acknowledged that lncRNA expression is more strictly regulated than mRNA. A small portion of lncRNAs expresses polypeptide products, much like mRNA does. As a result, lncRNA function mechanisms are extremely complex. Since the number of lncRNA genes exceeds protein-coding genes, lncRNAs are more stable than mRNA, so they are more suitable. All in all, lncRNAs open a new door for clinical diagnosis and treatment of breast cancer.

Keywords: LncRNA, Epigenetic, Brest Cancer

Investigating the Role of Gene Therapy in Breast Cancer (Review)

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Introduction: Breast cancer is the most common female malignancy in the United States. Breast cancer affects one in nine women in the United States. Yearly, 46,000 women die from breast cancer, despite early detection methods and advanced conventional treatments. Gene/prodrug systems can be used to selectively target malignant cancer cells while leaving normal cells unharmed. Thus, the application of these systems to reduce undesirable side effects has recently received increased attention. A gene therapeutic system using cytosine deaminase (CD)/5-fluorocytosine (5-FC). a gene-directed enzyme/prodrug therapy (GEPT) that currently exists, involves the conversion of a nontoxic drug (5-FC) into the toxic metabolite 5-fluorouracil (5-FU), an active anticancer drug that inhibits DNA synthesis in cancer cells. In addition, herpes simplex virus thymidine kinase (HSV-TK) suicide gene and its complementary prodrug ganciclovir (GCV) have been used to selectively target human types of cancers, indicating a potential therapeutic use of this gene delivery for primary human types of cancers. This GEPT system has been used to treat various types of cancer including colorectal and prostate cancer in clinical trials. In addition, CPT-11, which is hydrolyzed into a topoisomerase 1 inhibitor (SN-38) by carboxyl esterase (CE), has been administered to cancer patients, including ones with colorectal cancer for decades. Prodrugs appear to be associated with reduced toxicity in normal tissues but there are potential problems with exogenous enzyme delivery for selectively targeting tumor cells. The aim of this study was to investigate the Role of Gene Therapy In Breast Cancer.

Methods: This review study whit Investigating the role of gene therapy in breast cancer has written the from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The wide range of delivery technologies now available have been explored in order to vehicle several classes of gene-based therapeutic agents. As distinct genetic alterations and gene expression profiles differentially affect the development and progression of breast cancer, correction of defective genes and regulation of gene expression through gene therapy has emerged as an innovative treatment strategy for breast cancer. Several approaches to induce genetic modification of a target cell have been evaluated, including transferring genes, segments of genes, or oligonucleotides such as siRNAs

and miRNAs.The more classical view in gene therapy for cancer and other diseases was represented by the replacement of mutated genes with their normal counterparts. Indeed, loss-of-function mutations in tumor suppressor genes have been identified as key events in breast cancer, with subsequent uncontrolled tumor progression and onset of metastasis. Therefore, the transfection of cancer cells with completely functional tumor suppressor genes (e.g. TP53) has been investigated as an anticancer strategy with both viral vectors and few nanosystems, resulting in inhibition of breast tumor growth and apoptosis induction. Recent advancement in the genome editing systems has led to a significant increase of the efficiency and specificity of gene targeting using site-specific endonucleases, including ZFNs, TALENs, and CRIPR/Cas9. ZFPs and TALENs, which are composed of a customized DNA-binding module and a non-specific DNA cleavage domain, can generate multiple genetic modifications by inducing DNA double-strand breaks (DSBs) that stimulate the error-prone non-homologous end joining or the more specific homologous recombination pathways.

Conclusion: A variety of gene therapy approaches have been evaluated for treatment of breast carcinoma. The majority of clinical trials focus on the p53 TSG. The preferred way of administration is the intratumoral injection of an adenovirus p53 vector. Despite the observed higher transgene expression with the adenoviral vectors, clinical evidence of tumor regression occurred only in a small minority of patients. It is clear that gene therapy of breast cancer is a very difficult undertaking. The results of breast cancer gene therapy clinical trials to date have demonstrated little toxicity. However, the rate of clinical response has been low to date and efficient transgene expression remains to be challenge. In this regard, future research needs to focus not only on novel strategies and transgenes, but also on the development of novel gene transfer vectors to help overcome this inefficiency. The immediate future of breast cancer gene therapy would suggest increasing success in using cancer gene therapy as adjunct therapy in local control of many cancers.

Keywords: Gene Therapy, Breast Cancer, malignant

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Investigating the Role of Gene Therapy in Breast Cancer (Review)

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1. ISLAMIC AZAD UNIVERSITY OF FALAVARJAN BRANCH

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and miRNAs.The more classical view in gene therapy for cancer and other diseases was represented by the replacement of mutated genes with their normal counterparts. Indeed, loss-of-function mutations in tumor suppressor genes have been identified as key events in breast cancer, with subsequent uncontrolled tumor progression and onset of metastasis. Therefore, the transfection of cancer cells with completely functional tumor suppressor genes (e.g. TP53) has been investigated as an anticancer strategy with both viral vectors and a few nanosystems, resulting in the inhibition of breast tumor growth and apoptosis induction. Recent advancement in genome editing systems has led to a significant increase in the efficiency and specificity of gene targeting using site-specific endonucleases, including ZFNs, TALENs, and CRIPR/Cas9. ZFPs and TALENs, which are composed of a customized DNA-binding module and a non-specific DNA cleavage domain, can generate multiple genetic modifications by inducing DNA double-strand breaks (DSBs) that stimulate the error-prone non-homologous end joining or the more specific homologous recombination pathways.

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Keywords: Gene Therapy, Breast Cancer, malignant

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Investigating the role of NGS technology and its applications in the medical industry (Review)

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Introduction: Since the completion of the Human Genome Project in 2003, there have been significant advances in genome sequencing technologies that have led to a reduction in costs and an increase in the number and diversity of sequenced genes. This method maximizes the number of sequenced bases in minimum time and generates a large amount of data and can be used to understand very complex phenotypes. This method enables researchers and doctors to build a variety of tools for examining the genome with high precision, which leads to an increase in our understanding of how gene variants cause phenotypes and diseases. NGS technology is becoming a common and versatile tool for biological and medical research. The high resolution and detection power of NGS enables us to pursue discoveries that were not possible with previous technologies. The use of NGS technology for complete DNA sequencing of cancer genomes has the potential to provide major advances in human understanding of the origin and evolution of cancer. NGS is an intensive parallel sequencing method that enables the sequencing of a large number of DNA fragments simultaneously in a single reaction. The amount of sequencing information by Sanger sequencing, which required years of time, was done with the NGS method in just a few weeks. In this article, an attempt has been made to examine the role of NGS technology and its applications in the medical industry by referring to the studies conducted in this field.

Methods: NGS method is used to screen a number of genetic diseases in babies. For example, this method is used for the accurate screening of Cystic Fibrosis (CS) in babies. The higher sensitivity of NGS for screening carriers of recessive disorders allows the detection of mutations in a larger number of individuals at a lower cost. The non-invasive application of NGS to detect genetic abnormalities in fetal development is rapidly developing. Today, NGS technology is used to screen for Down's syndrome, Pato's, Edward's and aneuploidy of sex chromosomes and some other disorders. The detection rate of Down syndrome with this method is more than 99%. These advances have

highlighted the potential of using NGS as a standard method for prenatal screening and other clinical screening tests.

Results: The genetic nature of cancer has led to the use of NGS as a useful tool in cancer diagnosis. Also, this technology should be provided for the detection of mutations (for example, BRCA1) in people who are considered high-risk groups for cancer due to their family history. Currently, multigene cancer panels are available for re-evaluation of cancer and the information needed to determine appropriate treatment methods. Examining the response to specific treatment of each individual can be done when combined with NGS data. The information obtained from NGS can be used to avoid treatments that are accompanied by multiple complications in certain patients, and also specific treatments with high potential of success can be selected to avoid the pain and suffering and cost of performing treatment methods. It reduced the inappropriateness. Targeted treatments are now available for some types of cancer, and specific genetic changes in tumor cells are revealed based on NGS data. For example, the use of Imatinib Mesylate for CML patients, Panitumumab for clonorrectal cancer and Erlotinib for lung cancer can be mentioned. Since it is possible to develop resistance to chemotherapy agents, a targeted treatment process based on genomic information is very useful in these cases.

Conclusion: In the last decade, with the advent of Next Generation Sequencing (NGS) sequencing technology, the sequencing of genes and the diagnosis of genetic diseases have undergone a huge transformation. In this article, an attempt was made to review the role of NGS and its applications in the medical industry by referring to the studies conducted in this field.

Keywords: NGS, technology, sequencing, genetic diseases, medical industry

Investigating the use of bacterial peptides as anticancer drugs with emphasis on p28 peptide of Pseudomonas aeruginosa (Review)

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Introduction: The second leading cause of death in the world in 2018 was cancer. Despite the advances in diagnosis and treatment, cancer is one of the most important causes of death. The main problem in cancer treatment is the adverse effects of chemotherapy and radiation and lack of response to drug treatment in some malignancies. Therefore, it is crucial to conduct research to find new anticancer agents. Azurin and exotoxin A from Pseudomonas aeruginosa, Pep27anal2 from Streptococcus pneumoniae, diphtheria toxin from Corynebacterium diphtheriae, and Entap from Enterococcus sp. all have anticancer effects. Coley toxins, which refer to Streptococcus pyogenes, Serratia marcescens and their metabolites, were successfully used by William Coley in 1909 to treat cancer and unresectable tumors. The increase of TNF-α and the activation of lymphocytes and macrophages is the main reason for the anti-cancer activity and therapeutic use of these toxins. Proliferation of pathogenic microorganisms in hypoxic cancerous lesions stimulates the patient's immune system and inhibits the cancer progression. After binding to p53, p28 peptide from the azurin protein of Pseudomonas aeruginosa exhibits anticancer properties. Binding of p28 protein to DNA binding domain (DBD) and formation of p28-DBD complex causes tumor regression. So, in this short article, the mechanism of anti-cancer activity of p28 peptide has been reviewed.

Methods: The p28 peptide selectively enters human cancer cells through endocytosis via the caveolin receptor. Selective penetration occurs at neutral pH and is protected against intracellular protease or endonuclease. Since, Azurin-p28 is absorbed using energy and without the involvement of membrane glycosaminoglycans, the p28 peptide is also used to deliver other peptides to cancer cells. The p28 peptide’s aa terminal roles in reducing cell proliferation and boosting apoptotic activity. Azurin-p28 can affect pathways of cancer signaling. By lowering or blocking VEGFR2 tyrosine kinase activity and phosphorylation, p28 prevents the angiogenesis of null tumors. The p28

peptide prevent the binding of constitutional morphogenic protein (Cop1), which is one of E3 ubiquitin ligases, with the DBD of p53 protein, and by reduction of ubiquitination and proteasomal degradation of p53 protein, they lead to a higher post-translational level of p53. The p53 protein is a tumor suppressor that inhibits tumor cell proliferation, participates in apoptosis, and regulates target gene transcription. Mouse double minute 2 (Mdm2) E3 ubiquitin ligase regulates degradation of the p53 protein by binding to its N-terminal activation domain (TAD).

Results: Since p28 peptide interacts directly with p53 tumor suppressor protein, it can be considered as a peptide with anticancer potential. Information about the DBD-p28 complex can reveal the function of p28 in regulating the anticancer effect of p53 protein, as well as the need to design new drugs that maintain the anticancer function of p53. Because as a result of post-translational stabilization of p53 against stress signals, the amount of this protein increases, the transcription of genes responsible for DNA repair increases and apoptosis occurs. Therefore, it can prevent cancers.

Conclusion: In conclusion, bacterial peptide p28, which is derived from azurin protein of Pseudomonas aeruginosa, can be used as an antitumor peptide and anticancer drug.

Keywords: P28, Azurin protein, P53, Pseudomonas aeruginosa, cancer

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Investigation of key genes involved in Alzheimer's disease by PPI network (Research Paper)

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Introduction: Alzheimer's disease is the main cause of dementia among older adults. This disease was first reported by Alois Alzheimer in 1906. The most common and characteristic lesions in the patient's brain are senile neural plaques and neurofibrillary tangles. Despite the fact that science is developing rapidly, no drug or treatment for Alzheimer's disease has yet been introduced or proposed. An organism's protein-protein interaction (PPI) network serves as a skeleton for its signaling circuitry, which mediates cellular response to environmental and genetic cues. In this research, we used protein-protein interaction networks to identify and introduce important and key genes that play crucial roles in Alzheimer's disease.

Methods: In the first step, we selected the suitable access code for Alzheimer's disease through the GEO site. GEO2R (https://www.ncbi.nlm.nih.gov/geo/geo2r/) was used to screen the DEGs in Alzheimer's tumor tissues and non-tumor tissues. For analysis, p-value <0.05 and fold change (|FC|)>1 were set as the cutoff criterion to select DEGs. In the next step, using the STRING-DB.org site, the interaction network of proteins was drawn and the output file was saved in TSV format, then the output file was opened using the Cytoscape software and then, the hub genes were identified

Results: The access code selected for the study was GSE5281 with 161 samples (tumor and normal tissues). In this dataset, brain samples from three Alzheimer's Disease Centers (ADCs) had been collected, and the expression profile was Affymetrix U133 Plus 2.0 array. The final protein interaction network that was drawn using the Cytoscape software had 188 nodes and 646 edges. among these 188 nodes, 10 main genes (CD44,NCAM1, ERBB2,PECAM1, SRC, CTLA4 ,CD28, FGF2, ,IL18,CRP) were hub genes in Alzheimer's disease

Conclusion: In this project, by the protein interaction network and Cytoscape software, 10 key genes related to Alzheimer's disease were obtained, but for further investigations, it is better that these genes are subjected to experimental tests.

Keywords: Alzheimer, PPI, key genes, Cytoscape, Node

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Investigation of nurse-led diabetes self-management training (Review)

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Introduction: Diabetes is one of the most common chronic diseases worldwide that threatens the health of society. Diabetes has a significant impact on the quality of life and today represents a real risk on a global scale due to the complications and diseases associated with this pathology. Hyperglycemia (high blood sugar) is a common feature of this disease. The average incidence in adults is 8.8%, and according to statistics, one in five Iranians suffers from diabetes or is at high risk of developing it. Early complications of diabetes include damage to the small blood vessels in the eyes, kidneys and nervous system, which can lead to vision problems and even blindness, kidney disease, neuropathy and the risk of amputation. Diabetes self-care refers to the process by which patients learn to live with the complications of diabetes in their social environment. Self-care is expressed in the patient's ability to adhere to recommended behaviors, such as compliance with medication regimen, a diabetic diet and active physical activity. Research has shown that nurses are more likely to promote preventive behaviors when seeking health care compared to other healthcare workers. Nurses are in a unique position to influence positive change and transformation in healthcare by acting as a bridge between theory and practice. Despite great efforts, there is little evidence on the clinical effectiveness of diabetes self-management interventions for glycemic control performed by nurses, especially in Iran. In this review, we focused on the impact of diabetes self-management education provided by nurses.

Methods: The present study is a review study with the aim of investigating the effect of nurse-led diabetes self-management education. The data of this study were collected from PubMed, ScienceDirect, and Google Scholar databases. The search was done using the keywords Effect, Nurse-Led, Diabetes, Self-Management and Education. In the initial search, 40 articles were found, and after evaluating the title and abstract, 18 articles were selected with the necessary conditions to participate in the present study, and general conclusions were made based on the information in the selected articles.

Results: Diabetes is a chronic disease that self-management and follow-up causes fewer complications for the patient. Self-management is the process of actively engaging in self-care activities with the goal of improving behaviors and well-being. Providing health education by nurses to diabetic patients increases awareness, changes behavior in preventing diabetes complications, increases self-efficacy, increases self-care activities (diet management, physical activity, blood sugar level monitoring and foot care). By applying specialized knowledge and skills and integrating competencies as educators, researchers, counselors, and leaders, nurses positively impact the delivery of health care services. The nurse plays an important role in increasing the patient's compliance with the management or treatment of any disease experienced by the patient. Support for improved adherence can be provided through educational interventions, which provide the clinical context for diabetes nurses to provide remote coaching and personal care while closely monitoring patients' progress.

Conclusion: Various methods of health education by nurses are now having a positive impact on improving and expanding self-care management and efforts to prevent diabetes complications, as well as on patient care by nurses, both directly and in communication with the patient and indirectly. This is possible by using the Internet for webinars or programs and brings tangible results in preventing diabetes complications and improving the quality of life of patients. With an increase of searches related to health promotion, it appears that nurses have yet to demonstrate a clear and obvious role in implementing health promotion activities. Rather, nurses can be viewed as public health promoters whose health promotion activities are based on correct knowledge and information delivery to patients. Nursing is a health-promoting profession, but several barriers related to organizational culture have a significant impact on the delivery of services.

Keywords: Nurse-Led, Diabetes, Self-Management , Education, Nurse

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Investigation of the effect of some aromatic compounds on the aggregation of alpha-synuclein protein using split luciferase complementary assay (Research Paper)

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Introduction: Parkinson's disease is one of the common neurodegenerative diseases among the elderly, one of the causes of this disease is aggregation and accumulation of alpha-synuclein protein. This protein is present in the nerve terminals of the brain, and if it aggregates and creates Lewy bodies, it causes the loss of dopaminergic neurons in the substantia nigra region of the brain and leads to the symptoms of Parkinson's disease. Recently, in order to improve Parkinson's disease, targeting this protein to inhibit its aggregation has been considered, and various inhibitors such as polyphenolic compounds, nanomaterials, etc. have been proposed. The bioluminescent system is used to analyze and report biological processes. This is due to high quantum efficiency and photon emission. Complementation of luciferase fragments is one of the techniques to investigate the interaction between proteins.

Methods: In this research, the effect of selected aromatic compounds on the aggregation of alpha-synuclein protein has been investigated using the split luciferase technique. The gene related to alpha-synuclein protein (A53T mutation) is connected to Nluc and Cluc gene fragments, and after expression, the reconstitution of luciferase activity was observed.

Results: In this research, 3 investigated compounds (A2, A3, A4) were individually affected after the transfection of the mentioned gene constructs on the HEK293T cell line. By examining the amount of luciferase activity after cell lysis, it was found that A3 has a significant effect on reducing the luciferase activity of the mentioned constructs and thus preventing the aggregation of alpha-synuclein protein.

Conclusion: Our findings suggest the need for further investigation on the capability of this aromatic compound in passing through the BBB and also on the effects of it on αS aggregation in animal models.

Keywords: parkinson disease, alpha-synuclein, protein aggregation, luciferase, aromatic compounds

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Investigation of the frequency of the SHV bla gene in Acinetobacter baumannii isolates from different departments of a general hospital (Research Paper)

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Introduction: Acinetobacter baumannii is one of the gram-negative and non-fermenting bacteria that cause opportunistic infections, especially in hospitals. Due to the emergence of resistance of this bacterium to all types of antibiotics, the periodic study of the resistance pattern is of particular importance. The aim of this study is to determine the frequency of the ESBL gene (SHV) in Acinetobacter baumannii over a period of 6 months.

Methods: This study was carried out on 105 isolates of Acinetobacter baumannii collected from different departments of a general hospital over a period of 6 months. The frequency of the SHV gene was tested by PCR.

Results: Of a total of 105 isolates, 77 (73.33%) were reported as SHV gene resistant.

Conclusion: The spread of ESBL isolates is increasing and represents a major challenge for the treatment of many diseases in the future. Considering that microbial resistance is increasing in the world and especially in Iran, studying the resistance pattern of hospital bacteria is of great importance..

Keywords: SHV ،ESBL, Acinetobacter baumannii

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Investigation of the frequency of VKORC1 gene polymorphisms in patients treated with warfarin in Rafsanjan city (Research Paper)

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Introduction: For more than 50 years, warfarin remained the main oral anticoagulant in patients with heart valve implants, atrial fibrillation, pulmonary embolism, thrombosis or thromboembolism, and dilated cardiomyopathy worldwide. Variability in response to warfarin is one of the main obstacles to its use in clinical practice. The required dose of warfarin varies between patients by up to 30-fold, and in general, women require a lower dose than men. In general, the bleeding complication during warfarin treatment is the most common adverse drug reaction with fatal or debilitating consequences, its overdose often leads to bleeding, and its underuse puts patients at high risk of thrombotic events. Warfarin is fundamentally affected by drug interactions, alcohol consumption and some nutritional supplements. In several studies, it was found that the intake of vitamin K is related to the dose. In addition, the required dose of warfarin in different people is also influenced by non-genetic factors. such as age, gender, weight, race, diet, height, smoking, drug use, and genetic factors such as: Two genes (CYP2C9 and VKORC1),)Cytochrome P-450 family 2, subfamily C, polypeptide 9 (CYP2C9) and vitamin K epoxide reductase complex, and subunit 1 (VKORC1) genes and VKORC1 genotypes(.Clinically, the optimal dose is estimated using blood coagulation tests, usually the international normalized ratio (INR). Drug metabolism varies from one patient to another due to genetic differences. The first clues to a genetic factor in this variation appeared in the 1990s. Currently, genetic differences can explain about 50% of the interindividual variability in warfarin treatment. Each population has its own gene polymorphism, which is considered as a determining factor in drug metabolism. Overall, VKORC1 variants could explain approximately 20-30% of the variation in warfarin dose. As a result, haplotype maps of common VKORC1 SNPs were created. The present study examined the frequency of VKORC1 gene polymorphisms in patients treated with warfarin in Rafsanjan city.

Methods: In this cross-sectional study, determination of the polymorphism genotype -1369G>A was performed by PCR-RFLP method on 113 patients taking warfarin. Statistical analysis was done with SPSS version 25 software to check the relationship between the demographic data of the patients and the amount of warfarin consumption.

Results: After comparing the average dosage of warfarin, no statistically significant difference was observed in terms of age and gender in relation to this polymorphism, but genotype AA has the lowest and GG the highest dosage of warfarin in they showed the patients.

Conclusion: Optimizing the appropriate dose of warfarin for each person based on genetic and environmental factors, especially in the initial stage of use, leads to a reduction in the side effects of this drug and, as a result, a reduction in treatment costs for patients and hospitals. The present study showed that there is a significant relationship between VCORC1 polymorphisms and sensitivity to warfarin and side effects in patients treated with warfarin in Rafsanjan city. Despite achieving a statistically significant result in the identification of different polymorphisms, more studies on the effect of gene variants on drug consumption among patients should be done, because the identification of these variants and their effects may be used as an effective factor in dose estimation. In general, it can be concluded that the frequency of CYP2C9 and VKORC1 genes is different in different populations. Considering the role of CYP2C9 and VKORC1 genes, it can be stated that these two genes are more related to the changes of polymorphisms among patients and play an important role in determining the dose of warfarin used for treatment in each specific patient. Estimating the appropriate doses of warfarin to administer can help reduce the risk of over- or under-anticoagulation and subsequently the risk of thromboembolism or bleeding.

Keywords: Anticoagulant, Warfarin, Genetic polymorphism, VKORC1

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Investigation of the production, purification and binding ability of anti-FGF7 sdAb D53 antibody identified by phage display technique.

(Research Paper)

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Introduction: Fibroblast growth factor 7 (FGF7) is a member of the fibroblast growth factor (FGF) family. FGFs are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth. Therefore, inhibition of FGF7 can be an effective treatment for such pathological diseases. In this study, we aimed to investigate the production, purification and binding ability of single domain anti-FGF7 antibody (i.e., D53) identified by phage display technique against FGF7.

Methods: The DNA sequence of D53 antibody was modified to change stop codon present in CDR2 region of heavy variable chain to glutamine codon with site directed mutagenesis and then the corrected sequence was cloned into pGEX-6p-1 expression vector. The constructed vector was transformed into E.coli origami and the protein of interest was expressed and subsequently purified using Glutathione-Sepharose affinity column. The produced domain antibody was analyzed by SDS-PAGE and western blotting techniques. To assess the binding ability of the produced antibody toFGF7, ELISA experiment was performed. Molecular docking of D53 into FGF7 was conducted using Z-dock program.

Results: The D53 domain antibody was produced in bacterial expression system. The protein band at about 13 kDa on SDS-PAGE was attributed to sdAb of interest. The production of D53 domain antibody was confirmed by using western blotting technique. In ELISA experiment, the produced sdAb showed appropriate affinity towards FGF7. Docking data was analyzed in protein interaction calculator (PIC) web site and various interactions of FGF7 and D53 were investigated.

Conclusion: In the current work, anti-FGF7 sdAb D53 antibody was expressed in a prokaryotic system and the affinity of the purified protein was elucidated. The findings in the current study can be valuable in designing and developing new FGF7 inhibitors.

Keywords: CAF , FGF7, sdAb, Affinity Chromatography, Westorn blot

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Investigation of the antimicrobial effect of curcumin nanoparticles and Chouvil plant extract on methicillin-resistant Staphylococcus aureus (MRSA) isolates from wound infections (Research Paper)

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Introduction: Methicillin-resistant Staphylococcus aureus (MRSA) is one of the major causes of burn infections. This bacterium is resistant to many antibiotics, so finding new antimicrobial compounds such as plant extracts and nanoparticles is essential for controlling this bacterium. The plant extract of Chouvil and the nanoparticle of curcumin due to their antibacterial and anti-inflammatory properties can be a suitable candidate for replacing antibiotics. The aim of this study is to determine the effect of curcumin nanoparticles and Chouvil plant extract on the growth rate of bacteria and changes in eno gene expression in methicillin-resistant Staphylococcus aureus isolates separated from burn wound infections.

Methods: In this experimental study, the effects of Chouvil plant extract and curcumin nanoparticles on methicillin-resistant Staphylococcus aureus (MRSA) isolates separated from burn wound infections were examined. PCR genotyping was used to confirm MRSA strains. To investigate the effects of curcumin nanoparticles and Chouvil plant extract on bacterial growth rate, MIC assay was performed, and for the combination synergy, the FIC method was used. Relative changes in eno gene expression were examined using the Real-Time PCR technique, and cellular toxicity was evaluated using the MTT assay.

Results: According to the results , curcumin nanoparticles and Chouvil plant extract at a concentration of 625 µg/mL inhibited the growth of MRSA strains. The synergistic effect of curcumin nanoparticles and Chouvil plant extract was observed at a concentration of 312.5 µg/mL. The simultaneous use of both compounds or each one alone did not show significant cytotoxic effects on HDF skin cells at the mentioned concentrations. The combination of these two

compounds caused a decrease in eno gene expression in bacteria by 1.4 to 3.12 fold (compared to the control group).

Conclusion: Curcumin nanoparticles and Chouvil plant extract had acceptable antibacterial properties and caused a significant decrease in the growth of methicillin-resistant Staphylococcus aureus (MRSA) isolates separated from burn wound infections and a decrease in the expression of the pathogenic eno gene. Therefore, these compounds can be considered for the treatment of burn infections caused by MRSA bacteria.

Keywords: MRSA, Antibiotic resistance, Wound infections, Curcumin nanoparticles, Chouvil plant extract

Investigation of Toxic effect of Sputtered Gold Nanoparticles on Liver Cells (Research Paper)

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Introduction: Today, gold nanoparticles are widely used in medicine [1]. Nanoparticles as drug carriers have been investigated in several articles. The large surface-to-volume ratio of gold particles enables their surface to be coated with hundreds of molecules, including therapeutics, and targeting agents. Gold particles combined with therapeutic agents improve drug pharmacokinetics and provide controlled or sustained release properties. These factors make gold particles an attractive tool for drug and gene delivery [2, 3]. Gold is typically a neutral and non-toxic material. However, nanoparticles usually have different properties compared to the original material. Some articles have reported the toxicity and some non-toxicity of gold nanoparticles on other cells [4, 5]. This article investigates the effect of toxicity of gold nanoparticles prepared by the sputtering method on liver cells.

Methods: In sputtering, different metals are used to coat surfaces for SEM imaging. During the deposition, the gold nanometer is separated from the target and sticks to the glass wall of the chamber. In this research, nanoparticles were separated from the wall of the sputtering chamber. Then nanoparticles with different concentrations were prepared in PBS. Different doses of the solution containing gold nanoparticles were poured into the liver cells. Liver cells were previously cultured in 96-well plates. 5 microliters of solution containing nanoparticles with concentrations of 20 µg/ml and 10 µg/ml were added to the surface of the cells. After one hour, 0.5 ml of culture medium was added to the surface of the cells. The range of concentrations presented in the articles is reported in concentrations less than 100 µg/ml. After 12 and 24 hours of adding nanoparticles, the conditions of the cells were checked under a microscope.

Results: The distribution of gold nanoparticles with a concentration of 20 µg/ml is shown in Figure 1. The data show that the size of the obtained particles is in the range of 25-60 nm. At first, liver cells covered more than 70% of the surface of the wells. 12 hours later, the cells were observed to be aggregated and some of them were dead and separated from the surface and suspended in the liquid on the cell surface. After 24 hours, almost all the cells were removed from the surface and died. The results of the present experiments show that the nanoparticles produced by the sputtering method

in the range of 25-60 nm have lethal and toxic properties on liver cells. The same result is observed for a lower concentration of 10 µg/ml.

Conclusion: In this study, the toxicity effect of sputtered gold nanoparticles on liver cells was investigated. Tests show that in the range of 25-60 nm, gold particles have lethal and toxic effects on liver cells. In addition to their type, the toxic properties of nanoparticles also depend on their size, geometric shape, and surface properties. In the present study, only the reaction of dead and alive cells was investigated. In order to find the main cause of the toxicity of this type of particle, it is necessary to study the effects of size, geometric shape, and surface properties of the particles in more detail.

Keywords: Gold nanoparticle, Liver, toxicity, cell culture, Sputtering

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Investigation of VKORC1 Gene Polymorphism Prevalence and its Relationship with Warfarin dosage in Consuming Warfarin Patients in Sirjan city by PCR-RFLP (Research Paper)

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Introduction: Warfarin is one of the coumarin derivatives and the most common anticoagulant drug prescribed for the treatment and prevention of thromboembolic diseases, atrial fibrillation, and Warfarin is one of the most important oral anticoagulants that is prescribed according to the needs of people in the process of preventing blood coagulation. The need for different doses of warfarin in different people is dependent on age, sex, diet, medications and most importantly genetic factors, which are among the effective factors in determining the dose of warfarin. Some polymorphisms of the VKORC1 gene, which expresses the C1 subunit of VKOR vitamin K epoxide reductase, are responsible for resistance and sensitivity to warfarin. The present study examines the frequency of VKORC1 gene polymorphisms and its relationship with warfarin dosage in cardiac patients taking warfarin in Sirjan city.

Methods: In this cross-sectional descriptive study, genomic DNA was extracted from the blood samples of patients taking warfarin using the Carmania Pars Gene (K.P.G) kit, and the genotype of VKORC1 gene polymorphisms (-1639 G>A) was determined by PCR-RFLP method on 153 patients taking warfarin were performed. 1.5% agarose gel was used to confirm the size of the amplified DNA fragment. Statistical analysis was done with SPSS version 25 software to check the relationship between the demographic data of the patients and the amount of warfarin consumption.

Results: After comparing the average dose of warfarin in individuals, no statistically significant difference was observed in terms of the amount of warfarin dose with age in relation to this polymorphism and the dosage of warfarin according to gender, as well as the PT and INR parameters were reported to be the same in the studied subjects. However, genotype AA showed the highest and GA the lowest required dose of warfarin in patients.

Conclusion: Geographically, Iran is located between two Asian and European populations. Therefore, the existence of high ethnic diversity and genetic variants in Iran due to immigration and population flows is not far from mind. As a result, it is important to obtain the distribution pattern of genetic variants in different regions of Iran due to the effect of variants on drug dose sensitivity. Also, considering the inter-individual and inter-ethnic differences in the response to warfarin, the limited therapeutic range of warfarin and the lack of availability of sufficient information about VKORC1 gene polymorphisms in Iranian people, the present study aims to Investigation of VKORC1 gene polymorphisms was done in Sirjan city. It seems that the relationship between the amount of warfarin consumption depends on the alleles of other genes in addition to the mentioned polymorphism that their effect can be effective on the amount of consumption, also the environmental conditions can also have an effect that should be checked.

Keywords: Anticoagulant, Warfarin, Genetic polymorphisms, VKORC1 gene, PCR-RFLP

Investigation the therapeutic effect of alpha amanitin toxin on metastatic cancer cells (Review)

Zahra Shakoori,[1,*]

1.

Introduction: Cancer is a disorder in which some body cells grow uncontrollably due to genetic changes and spread to other parts of the body. Tumor suppressor genes are genes that limit the rate of cell division, control the time of cell death, correct DNA mistakes, and limit the growth rate of a cell and protect it from cancer. The mutation of these tumor suppressor genes can allow the cell to grow out of control and lead to tumor and cancer. The most common tumor suppressor gene that is mutated in cancer patients is P53 or TP53. In more than half of cancers, this gene is lost or damaged and turned into an oncogene. Oncogenes can turn a healthy cell into a cancer cell.

Methods: Researchers have gained a lot of information about how genes play a role in cancer. But many cancers are not related to a particular gene, and often not just one gene, but several genes are involved in causing cancer. What is discussed in this review article is TP53 and its neighboring gene called POLR2A. Studies have shown that the mutation and deletion of TP53 in cancer cells leads to the mutation and deletion of POLR2A due to the proximity and in this case the number of copies of POLR2A is reduced and drugs and toxins such as alpha-Amanitin (α-AMA), which is obtained from a type of poisonous mushroom called Amanita phalloides, will have a greater effect on cancer cells than normal cells. Mushrooms and their products play an important role in global trade as an important dietary component and are rapidly becoming an essential part of the world's diet. However, due to the popularity of fungi, thousands of cases of poisoning occur worldwide annually. Among them, the most toxic fungi are those containing amanitins (AMAs). α-AMA is a bicyclic octapeptide and a strong inhibitor of DNA-dependent RNA polymerase II, which inhibits RNA polymerase II by blocking the transfer of RNA and DNA.

Results: It can be said that this unique mechanism of destruction, which basically acts on rapidly growing cells and ultimately leads to cell death, is almost more distinct and effective in alpha-Amanitin than other toxic cargoes produced in a laboratory.

Conclusion: A low and safe dose of this toxin can be used for cancer treatment, so that in this low dose, normal cells are less damaged, and by

injecting a weak dose of this toxin, a suitable treatment can be created for cancer patients. With these findings, this research can provide a new perspective for the treatment of cancer using molecular and genetic methods and fungal toxins, and it is hoped that it will promise a new and long life treatment for cancer patients.

Keywords: POLR2A _ TP53_ Cancer_ alpha-Amanitin _ RNA polymerase II

Iranian Journal of Blood & Cancer (Review)

Narges Mardani,[1,*] Amin Soltanpor Dehkordi,[2] Maryam Sayahinouri,[3] Haniyeh Sadat Hosseininia,[4] Arman Saadati Partan,[5] Arasalan Jalili,[6]

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Introduction: According to the lastest WHO report, lung cancer ranks among the top cancer- associated mortalities. Morever, it has been related to a high rate of metastasis, which indicates the importance of Angiogenesis. Histologically, lung cancer is divided inti NSCLC and SCLC, with NSCLC being the most common. Angiogenesis is essential for tumor development. Additionally, immune cells, soluble factors, and ECM play a crucial role in their formation. this study reviews the angiogenesis formation factors in previous studies as well as analyzes in silico angiogenesis-related genes in NSCLCs.

Methods: First, three high-throughput GEO data sets with 18 lung cancer and normal samples were adopted to achieve the study purpose. Then, the up-and-down-regulated genes with p-value < 0.05 were isolated. Next, the genes were taken to the Enrichr and the KEGG databases. Lately, our in-silico analysis confirmed the gene expression connection between angiogenesis and lung cancer invasion.

Results: It is reported that EPhB2, PIK3R2, HSPB1 and Wnt7b is the most prevalent in NSCLC subtypes. Moreover, a decrease of 50% in overall survival in both low and high Wnt7b transcripts per million was observed.

Conclusion: In conclusion, the gene expression association between the development of angiogenesis and lung cancer invasion has been proven by in silico analysis. The most upregulated genes which showed high logfc in lung cancer in comparison with the healthy patient have been identified. Among them, Wnt7b, due to its high logfc, distinct regulation, and carcinogenesis, was chosen as the candidate. Furthermore, in silico analysis highlights Wnt7b's importance in tumor cells. This regulates angiogenesis, and

carcinogenesis, and is critical for normal lung tissue development. The violin plot (As shown in Figure 4) and overall survival graph (As shown in Figure 5) have demonstrated that the distinct role of Wnt7b in lung cancer needs more consideration. Our result has fully illuminated the significance of angiogenesis-related genes in lung cancer progression. In particular, Wnt7b plays a crucial role in regulating survival rates. In silico our analysis has shed light on the potential of Wnt7b in enhancing the overall survival rate. Finally, future in vitro and in vivo studies should provide a more reliable understanding of its regulatory function.

Keywords: Wn7tb EPhB2 Angiogenesis Lung cancer In silico Bioinformatics

just one extra chromosome; Down syndrome (Review)

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Introduction: Down syndrome is the most common cause of mental retardation with genetic origin. Most affected people have an extra chromosome 21. Of course, other things may also cause this disease, including; Robert Sonin translocation and isochromosomes. In recent years, the life expectancy of these people has increased, which increases the possibility of contracting secondary diseases at a later age. The incidence of this disease increases with the age of the mother. And according to the definition of the word syndrome, it has a variety of symptoms that are categorized and analyzed in this article.

Methods: Using the Google Scholar database, articles related to the topic were searched within the time limit of 2019 to 2023. Then, based on factors such as symptoms and new achievements in this field, they were categorized and analyzed. Search terms in this database: Down's syndrome/New findings of Down's syndrome/Down's syndrome and Alzheimer's/Down's syndrome and corona virus

Results: Trisomy of chromosome 21 is a primary genetic cause of developmental abnormalities that lead to learning and cognitive disabilities. History: Down syndrome was first described in 1866 by an English doctor named John Langdon Down. 100 years after this description, Dr. Jerome Lejeune in Paris was able to find the link between chromosome 21 and Down syndrome. signs: Congenital heart defects/ Abnormalities related to the digestive system/ Blood disorders/ Endocrine disorders/ Neurological disorders/ Skeletal disorders/ Vision and hearing disorders (All these cases have been reviewed and reviewed in this article.) Diagnosis or screening methods: Ultrasound (between 14 and 24 weeks of pregnancy)/increased thickness of nuchal folds/amniocentesis/sampling of chorionic villi/morphological changes of the nose (All these cases have been reviewed and reviewed in this article.) The possibility of contracting secondary diseases: Down syndrome and Alzheimer's disease: Almost all adults with Down syndrome show Alzheimer's neuropathological changes by the age of 40. As a result, dementia becomes more common with age. Down syndrome and epilepsy: people with this disease, especially in older age, are susceptible

to epilepsy, which is also related to Alzheimer's disease. Down syndrome and corona virus: these people are very vulnerable to immune system disorders, including autoimmune diseases, and also show more severe symptoms than other people during viral infections. The results of the research show that people with Down syndrome are known as a vulnerable group against Corona, who experience more severe symptoms with longer hospitalization periods.

Conclusion: Down syndrome is a disease with various symptoms that can cause problems in almost all organs and systems of the body. This disease can provide the basis for contracting other diseases. Many researches have been done in relation to the knowledge of the nature of the disease, but genetic counseling is expected to play a stronger role in preventing this syndrome. Also, more research should be done on how to manage the various symptoms of this disease.

Keywords: Down syndrome/Alzheimer/coronavirus/epilepsy

Kartagener syndrome review article (Review)

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Introduction: Kartagener's syndrome is described as autosomal recessive inherited syndrome. Primary (genetic) defects in the structure and function of sensory and motile cilia result in multiple ciliopathies. A reduction in the number of arms which propel mucus (dynein arms) is a common abnormality but many other structural defects of the cilia have been found.

Methods: Patients with normal cilia morphology but abnormal mucus propulsion have been detected. Symptoms of kartagener : inversion of the circulatory system and the viscera. This is an incorrect placement of the organs on the opposite side from the corresponding one. swelling of the sinuses, that is, the spaces inside the nose and head. dilation of the bronchi, which can cause asthma in patients. The important symptom that distinguishes Kartagener syndrome from other types of primary ciliary dyskinesia is the positioning of the internal organs on the side opposite from normal (called situs inversus). For example, the heart is on the right side of the chest instead of the left. The main symptom of Kartagener syndrome is lung problems. Because the cilia don’t work properly, you have trouble moving debris and fluid from your lungs. The severity of symptoms can vary for each person, but they usually start at birth. Primary ciliary dyskinesia is a genetic condition where the cilia aren't working properly.

Results: Cilia are hair-like structures on the surface of your cells and are found in your lungs, airways, and other areas. They move in a wave-like motion to help position organs during a baby's growth in the womb, and they help move out mucus, bacteria, and debris from your lungs and airways. (PCD) also known as Kartagener's syndrome can present with cough, multiple pneumonia, bronchiectasis, rhinosinusitis, infertility, among others, but it can rarely present with massive. In PCD and Kartagener syndrome, these cilia don't move or they don't move very well, which causes ongoing lung, sinus, and ear problems. Not all people with PCD have reversed organs, so Kartagener syndrome is a subtype of the disease. Disorders of ciliary motility may be congenital or acquired. Congenital disorders are labeled as PCDs. Nearly 50% of PCD patients have situs inversus. Such cases of PCD with situs inversus are known as Kartagener's syndrome. Male patients with KS

invariably present infertility, while women present reduced fertility.Infertility in male KS patients is due to diminished sperm motility, while in females it is due to defective ovum transport because of dyskinetic motion of oviductal cilia, suggesting that the ciliated endosalpinx is essential for human reproduction.

Conclusion: Normally, the diagnosis of Kartagener's Syndrome is complicated because it is a rare disease and each person shows some symptoms. There is no cure for Kartagener syndrome. The main treatments focus on keeping airways clear and loosening and getting rid of thick, extra fluid, mucus, and debris. It's also important to get vaccines to prevent serious disease from viruses.

Keywords: Kartagener - syndrome- PCD- cilia

key altered biological pathways in acute myeloid leukemia with and without FLT3 mutation (Research Paper)

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Introduction: FLT3 is one of the significant genes involved in Acute Myeloid Leukemia (AML), its activation results in apoptosis, proliferation, and differentiation of hematopoietic cells. It has two mutation hotspots which leads to constitutive activation and causing AML. The survival rate for FLT3 related AML is nearly double fold lower than wild type AML.

Methods: In this study, the dataset with GEO accession number GSE17855 has been used, the data analysis progressed with R using 50 wild type AML samples and 48 FLT3-related AML. The p-value was set on 0.01, resulted in 5000 genes. We Obtained approximately 200 hub genes using STRING and Cytoscape 3.6.0. once again using STRING and Gephi 0.9.5 the hubs of hub genes and its modules were obtained. After surveying genes on Enrichr, the joint pathways of five databases were obtained and analyzed.

Results: Top five down regulated genes were CTNNB1, UBB, UBE21, BIRC5 and FOXO3, and top five up regulated genes were JUN, EP300, TP53, FOS and MAPK14. These genes were mostly involved in CCKR signaling map, MAPK Family Signaling.

Conclusion: The treatment of patients with AML-FLT3, which is now done by inhibiting FLT3, has some complications; this study focuses on specifying downstream pathways which may help for more effective therapies.

Keywords: Acute myeloid leukemia, cancer, FLT3 related AML, AML, Microarray analysis

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Kindling model : a way to inducing epilepsy (Review)

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Introduction: Epilepsy is the fourth most common disease of the nervous system and if not treated, it leads to cognitive and behavioral disorders and permanent brain damage. Animal models are used to observe epilepsy mechanisms and discover new antiepileptic drugs. Today, there are different methods for inducing epilepsy in animal models and The mechanism of each method induces a different type of epilepsy. Researchers found that The best method for temporal lobe epilepsy is to use the kindling model which we are going to discuss in this review article. In the kindling model, repeated electrical stimulations are induced in different areas of the brain, especially the amygdala nuclei, and hippocampus, and depending on the type of animal and the location of the stimulation, it increases irritability and seizures. In the kindling model, it is possible to observe the pattern of epilepsy, but it is expensive and requires a prolonged procedure. The kindling stimulation usually begins with 100 μA, continued by daily increases of 200 μA until a localized AD is induced. The average time for electrical stimulations to become a. Generalized seizures is between 9_91 days.

Methods: Our review is based on literature searches in online medical databases, as well as some specialized books about epilepsy and also we use some science journals from 2000 to 2023. The phrases were used: “epilepsy, ” “kindling model,” “the role of the kindling model in epilepsy,” “animal models of epilepsy,” and” kindling model in simulation of epilepsy ”. And the keywords are, “kindling model, ” “epilepsy,” “temporal lobe’s epilepsy,” and “electrical stimulation ”. At the end of searching, we also checked every article’s references.

Results: After reviewing 21 articles, we realized that daily repeated electrical stimulation in animal modes eventually leads to longer and more intense focal and tonic-clonic seizures. The average daily number of electrical stimulations required to reach the final stage of generalized epilepsy is 36 days in cats. Daily repetition leads to prolonged discharges that gradually cause convulsive activity. Once an animal has successfully reached the final stage of a seizure, the increased response to the stimulus appears to be permanent, and spontaneous seizures can occur within a short period.

Conclusion: Kindling is an experimental model of partial seizures that leads to secondary generalization seizures, it happens by repeated low-intensity electrical stimulation in many different areas of the brain specifically the limbic system. Over 30 years, candling models became an efficient way to study multiple seizures in the animal's brain and compare it to the human's brain. It seems that kindling is not just a chronic model of epilepsy but, it's a tool for understanding the consequences of seizures which not have control. Investigators found out that the kindled animals in the limbic circuit have the most symmetry with humans.

Keywords: Keywords: kindling model, epilepsy, temporal lobe epilepsy, electrical stimulation

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Kissing disease and other Infectious mononucleosis review article (Review)

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Introduction: The Epstein-Barr virus is a fascinating human herpesvirus whose study has provided unique insight into host:pathogen interactions and complex cellular molecular processes. Epstein–Barr virus (EBV) is an oncogenic virus infecting more than 95% of the world's population. The virus is the first discovered human tumor virus . EBV was discovered 40 years ago from examining electron micrographs of cells cultured from Burkitt's lymphoma, a childhood tumour that is common in sub-Saharan Africa, where its unusual geographical distribution — which matches that of holoendemic malaria —indicated a viral aetiology. It is one of the members of the herpes virus that can infect humans. EBV — a γ-herpesvirus — was found to be in all human populations. Epstein-Barr virus is transmitted from person to person through body fluids, especially saliva.

Methods: This is why mononucleosis, one of the most famous infections associated with this virus, is commonly known as the kissing disease. But you can also get infected by sharing personal items such as toothbrushes or food containers with someone who has this virus in their body. In addition, the virus can be spread through blood and semen. After primary infection—responsible for infectious mononucleosis in young adults—the virus persists lifelong in the infected host, especially in memory B cells .One of the main symptoms of Epstein- Barr is fever, which can last for several weeks. In the early stages, these infections can be controlled, but if they progress, they can become more dangerous.

Results: The most common Epstein-Barr symptoms that teens and adults can experience include: fever feeling tired headache sore throat swollen lymph nodes in the neck or under the arms swollen tonsils enlarged spleen (splenomegaly) skin rash. these symptoms can last for 2 to 4 last for weeks, although fatigue may last for weeks or months.The continuing studies of EBV have identified additional cancers and diseases linked to EBV . EBV it can lead to cancers such as lymphoma or carcinoma. Recent reports also suggest a link between EBV infection and multiple sclerosis.

Conclusion: were used They showed for the first time that the IM attack rate increases significantly and exactly in relation to the usual age of onset of puberty. And the results they observed thatThe cumulative risk of IM before age 30 years was 13.3% for males and 22.4% for females. and predicted that IM is likely to become more common in the coming years through the latency of EBV infection.

Keywords: EBV VIRUS kissing disease Viral Hemoglobin

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KIT/hsa-miR-149-5p/MAGI2-AS3 axis affects Breast cancer development by regulating "Ras" signaling pathway: bioinformatics gene expression profiling (Research Paper)

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Introduction: Breast cancer (BC) is the most commonly diagnosed neoplasm in women worldwide. Among the effective biomarkers in cancer, we can mention miRNAs and lncRNAs. MiRNAs are taken into consideration master gene regulators. additionally, aberrant expression of many lncRNAs has been extensively located in breast cancer. In addition, the mRNA-miRNA-lncRNA axis interaction regulate gene expression. For this reason, it is very essential to study it.

Methods: In this article, an attempt has been made to find a network between genes, miRNAs and lncRNAs in BC, by using microarray methods and databases such as GSE in GEO, gene expression and survival in ENCORI, pathway in Enrichr, protein interactions in STRING, miRNAs in miRWalk, lncRNAs in lncBase v.3 and expression of lncRNAs in lnCAR.

Results: GSE134359 has been performed by using GEO2R and KIT gene with (adjusted P.Value 3.98E-23) and (log FC -7.16) has been selected from 946 genes. This gene encoding a tyrosine kinase receptor and plays a role in many cell types. types of RNAs have been found and investigated. Such as hsa-miR-149-5p with (binding energy -32.2), (coefficient-r -0.182), (HR 0.97) and (log-Rank p 0.83), hsa-miR-671-5p with (binding energy -31.5), (coefficient-r 0.206), (HR 1.15) and (log-Rank p 0.4) which are significantly overexpressed or MAGI2-AS3 lncRNA with (log FC -5.7974) and ZNF436-AS1 lncRNA with (log FC -4.5338) which are downregulated.

Conclusion: Therefore, the results of this study indicate that there might be a communication between this network and BC and reinforces the possibility that KIT is an authentic biomarker for detecting cancer cells. Also, the Ras signaling pathway has been checked, which showed that the KIT plays a role in it. So, it can be assumed that KIT/hsa-miR-149-5p/MAGI2-AS3 and KIT/hsa-miR-671-5p/ZNF436-AS1 axes can be involved in regulating the

function of this pathway. Discovering these connections, will help us to know more about the causes of BC as well as finding new solutions and treatments.

Keywords: Breast cancer, KIT, miRNA, lncRNA

Knockdown of Long Non-coding RNA NEAT1 Improves Drug Efficiency in Ovarian Cancer (Review)

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Introduction: Ovarian cancer is a malignancy of the female reproductive system and is the third most common cancer among all cancers in women. Due to the fact patients are diagnosed in advanced stages, it is the fifth cause of cancer death among women. Despite the emergence of different new and advanced therapeutic approaches, debulking surgery and chemotherapy are the most common treatments. In addition to other therapeutic challenges, drug resistance is still an obstacle in ovarian cancer treatment. Hence, it is required to investigate more in the field of target therapy and find new probable targets. long non-coding RNAs (lncRNAs) are a kind of non-coding RNAs of length exceeding 200 nucleotides. LncRNAs have a crucial modulatory role in various biological processes such as growth, differentiation, chromatin remodeling, etc., consistent with their broad-spectrum expression pattern, their acceptable balance in body fluids such as urine and plasma, and cell-specificity. Changes in their expression levels and numerous mechanisms are the reasons that lncRNAs cause cancer by undergoing them.

Methods: In this paper, we searched ISI Web of Science, PubMed, Scholar, Scopus, and Science Direct for literature reports on NEAT1 in OC, and articles published until 2023 were considered. The search terms used in the review include “ovarian cancer”, “long non-coding RNA”, and “NEAT1”.

Results: Nuclear Para speckle assembly transcript 1 (NEAT1), is an imperative structural component to the creation of paraspeckles, which regulates various gene expressions. In addition to the usual characteristics of lncRANAs, NEAT1 is involved in the advent of the corpus luteum, placenta, mammary glands, immune response, and multiple diseases, including cancers specifically ovarian cancer. The role of NEAT1 in ovarian cancer has

been investigated by previous studies. Reported results indicate the high expression levels of NEAT1 in ovarian cancer patients and pinpoint the oncogenic feature of NEAT1 in this cancer. Meanwhile, resistance to drugs used in chemotherapy is a major problem associated with NEAT1. This unfortunate outcome occurs due to interactions between NEAT1 and various miRNAs, as well as proteins.

Conclusion: In this review we described the molecular mechanisms of NEAT1-involved drug resistance in OC, indicating a valuable target to overcome drug resistance and improve therapeutic outcomes in ovarian cancer patients.

Keywords: Ovarian cancer (OC); Long non-coding RNA (lncRNA); Drug resistance; NEAT1; target therapy

Lassa fever disease review article (Review)

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Introduction: Introduction: Lassa fever(LF), The cause of acute viral hemorrhagic disease is the Lassa virus (LASV). Exposure toMastomys natalensis, the rodent host, contaminated feces or urine, is the primary cause of infections in humans.Environmental elements, such as being close to vegetation, forests, and garbage, enhanced the likelihood of LASV exposure The family Arenaviridae includes the virus that causes Lassa fever Lassa fever has been linked to several rodent species, including Hylomyscus pamfi and Mastomys erythroleucus.Every year, LAV results in 5,000 fatalities.Since 2010, there have been more documented cases of LF.

Methods: Material methods: The Lassa virus (LASV), a single-stranded RNA arenavirus encapsulated, bipartite, is what causes Lassa fever This RNA virus has a typical diameter of 110 to 130 nm and has a spherical or rounded shape The smaller segment's precursor nucleoprotein and glycoprotein, as well as the more significant segment's RNA-dependent RNA-polymerase and matrix RING Zincfinger protein, are the four proteins that the RNA .genomes encode virulence and pathogenesis factors LASV is a negative-sense, single-stranded RNA virus with an envelope. The large and small parts of the genome each contain two ambisense regions.

Results: Results: Negative effects from Lassa virus infection are particularly likely to affect pregnant women and their .unborn children According to a recent assessment, pregnant women have a three times higher chance of dying from Lassa .fever than non-pregnant women Factors Affecting the Reemergence of Epidemics of Lassa Fever Migration, travel, and nosocomial transmission Systems of public health Environment and Climate Effects of Conflicts and Civil War

Conclusion: Conclusion: Poor outcomes among Lassa fever virus-infected pregnant women are mostly brought about by immune changes during pregnancy or the virus' attraction to the highly vascularized placenta. The patient's prognosis could get worse if medical treatment is postponed. Additionally, overlapping clinical symptoms including headaches, vaginal

bleeding, and tummy pain in pregnant women might make it difficult to diagnose Lassa fever Particularly in endemic locations, the ecology of the Lassa virus and its interaction with humans, as well as the development of Lassa fever, are complex. At the moment, ribavirin, an antiviral medication, is . the only available specialized treatment.

Keywords: Lassa fever(LF),stable signal peptide (SSP) ,pathogenesis, ribavirin, infectionstable

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Legionnaires disease review article (Review)

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Introduction: Mild to severe pneumonia can result from legionnaires' disease. Legionella species are typically found in contaminated soil and water sources. The summer and fall seasons are when the breakouts typically take place. Respiratory and gastrointestinal symptoms, hyponatremia, and transaminitis are common clinical signs that point to Legionnaires' illness. We describe a patient who developed Legionnaires' illness after becoming overheated. Typically, 2 to 14 days after bacterial exposure, the symptoms appear. This illness shares several characteristics with typical community-acquired pneumonia. Fever, coughing, dyspnea, headaches, and muscle aches are among the typical symptoms.

Methods: From the patient's sputum, Legionella pneumophila strain Corby was identified. Due to coughing and expectoration for five months and worsening shortness of breath for one and a half months, the patient was admitted to the hospital for 21 days. For bacterial isolation, peripheral blood, sputum, and bronchoalveolar lavage fluid (BALF) were collected. White blood cell count, neutrophil percentage, C-reactive protein, Next-generation sequencing (NGS) data (peripheral blood, bronchoalveolar lavage fluid, and bronchial brushing specimens), and the results computed tomography (CT) data were obtained as part of the patient's clinical information.

Results: The Corby clinical isolate's antibiotic sensitivity was tested. Nine drugs, including ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, azithromycin, clarithromycin, rifampicin, tigecycline, and doxycycline, were shown to be sensitive to the strain, according to the results. The amount of intracellularly developing L. pneumophila strains Corby and Philadelphia 1 (JR32) was counted after 1.5 hours of co-culture with murine macrophage J774. According to the findings, Corby (ICDC) has a higher capacity for intracellular proliferation than JR32. There were noticeably more intracellular bacteria in the Corby group than in the JR32 group 48 and 72 hours after infection

Conclusion: In the summer and fall, outbreaks of legionellosis are frequent. The illness might cause the involvement of multiple organ systems or just simple pneumonia. High suspicion, prompt diagnosis, and prompt treatment

have led to better results, such as faster symptom clearance, shorter hospital stays, and lower mortality. The disease commonly manifests as gastrointestinal and respiratory symptoms, and according to the literature study, it is typically contracted from drinking water that has been tainted.

Keywords: Legionella pneumophila, pontiac fever,legionellosis,Legionnaires disease, epidemiology

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Leishmaniasis treatment with nanotechnology (Review)

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Introduction: In 98 countries, leishmaniasis is endemic, putting 350 million people at risk such as Africa, Asia, Southern Europe, and Central and South America. In brief, visceral leishmaniasis (VL) and cutaneous leishmaniasis (CL) are two major manifestations of a complex of parasitic diseases. A majority of chemotherapy consists of pentavalent liposomes of amphotericin B, antimonials, and miltefosine. In the face of several limitations, the effectiveness of the current antileishmanial agents has remained inadequate for treating leishmaniasis, Including toxicity, low efficacy, negative side effects, lengths of treatment, drug resistance, and the cost of treatment. By optimizing the metabolism, adsorption, distribution, and excretion of existing drugs using nanotechnology, we can improve leishmaniasis treatment through improved drug delivery systems, as well as reducing their toxicity. An overview of nanotechnology-based antileishmanial drug delivery systems will be presented in this review.

Methods: In the years 2000 to 2020, it has been possible to retrieve published research data from several universally recognized databases, such as PubMed, Scopus, Science Direct, and Google Scholar, by means of several universally recognized databases. Downloading and retrieving published literature on nanotechnology in leishmaniasis treatment was the search strategy. In this study, keywords such as "nanomedicine in leishmaniasis treatment," "nanoparticle-based therapies for leishmaniasis," "nanoparticle drug delivery for leishmaniasis "nanotechnology against Leishmania parasites," and "nanoscale treatments for leishmaniasis infection" were used. The number of studies found was 10,000. Nine thousand studies were excluded based on abstracts, and 300 were read in full. The study included 50 relevant articles. With the advancement of nanotechnology,

several innovative treatments and drug delivery systems have been developed to combat leishmaniasis.

Results: Anti-leishmanial agents can be delivered intracellularly using the Nanocarrier in macrophages located in the spleen, liver, and bone marrow of mice, allowing them to concentrate locally at parasites, resulting in lower, more effective doses, improved treatment outcomes, and reduced toxicity. Furthermore, they have been designed to ensure the drug release profile remains constant so that the parasite is continually exposed to the drug. Additionally, nanocarriers can be used for drug delivery via more patient-friendly routes (oral, nasal, topical) as well as for preventing degradation of the active substance in vivo. Water solubility is a problem with many molecules approved for development as antileishmanial drugs. Over the past decade, several interesting nanoparticle-based biosensors have been developed for the diagnosis, treatment, and prevention of leishmaniasis (e.g., silver nanoparticles, gold nanoparticles, metal oxide nanoparticles, QDs, etc.). In addition, researchers have explored nanocarriers (e.g., PLGA and CS nanoparticles, SLNs, liposomes inorganic nanocarriers, etc.). The combination of reverse vaccinology and proteomics can be used to develop multi-epitope peptides (Induce cellular immunity by binding to the major histocompatibility complexes I and II molecules). Major histocompatibility complex-affinity antigens will be delivered with adjuvanted nanocarriers.

Conclusion: In addition to being more sensitive, specific, and reproducible, nanotechnology-based bioassays have also been shown to be more effective. The prophylactic and therapeutic use of numerous nanocarriers for a wide range of diseases has also demonstrated promising results in vivo. The results indicate that although nanoformulations could be used for the topical treatment of CL, only a very limited number have actually reached the stage of clinical development despite promising observations. Consequently, the development of nanoformulations based on this principle will require the collaboration of chemists, pharmaceutical scientists, biologists, engineers, experts in vaccinations, and bioinformatics professionals.

Keywords: Leishmaniasis Nanocarrier Nanoparticle Toxicity Nanotechnology

Limosilactobacillus reuteri review article (Review)

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Introduction: Over a century ago, Élie Metchnikoff brought beneficial lactic acid bacteria (LAB) into the scientific spotlight. He popularized the idea that LAB can prevent diseases and delay aging through the consumption of fermented dairy products. Fermented foods containing psychobiotics are of growing interest among food scientists.The phrase "healthy mind in healthy body" means that physical and mental systems are closely related. In other words, the health status of the body affects the mental status. Recent studies on the microbiota-intestinal-brain axis showed the interaction, correlation and relationship of the gut microbiota with the mental state of the host. Considering the digestive system, the health status of the gut, including the gut microbiota, may change the host's mind, because the gut microbiota It is described as the third organ. Among the indigenous and acquired resident members of the gut microbiota, certain psychoactive bacteria are defined as psychobiotics by Dinan et al. These are probiotics that affect and benefit the mental health of the host. The influence of gut microbiota on the gut-brain axis has been actively studied in microbiology. The association of gut microbiota with unstable mental health or disorders such as Alzheimer's disease, anxiety, depression, stress sensitivity, autism spectrum disorder, schizophrenia, and Parkinson's disease has been widely discussed in the last decade. The gut-brain axis was thought to be bidirectional, from the gut to the brain and from the brain to the gut.

Methods: The gut-brain axis was thought to be bidirectional, from the gut to the brain and from the brain to the gut. Therefore, the gut-gut-brain microbiota axis is a very interesting topic in the study of host microbiome interactions. One of the goals of researchers in this field is to improve the mental health of the host through the adjustment of microbiota or specific microbial supplements, which gives rise to the concept of psychobiotics. Psychobiotics are a special class of probiotics, which deliver mental health benefits to individuals. They differ from conventional probiotics in their ability to produce or stimulate the production of neurotransmitters, short-chain fatty acids, enteroendocrine hormones and anti-inflammatory cytokines. Owing to this potential, psychobiotics have a broad spectrum of applications ranging from mood and stress alleviation to being an adjuvant in therapeutic treatment for

various neurodevelopment and neurodegenerative disorders.Within the classification of neurodegenerative diseases, we find at least 100 different pathologies, which present specific symptomatology, with the most prevalent being Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS) .

Results: In addition to GABA production and immunomodulatory properties, L. reuteri DSM 17938 has other mechanisms that may contribute to its psychoactive effects.

Conclusion: The gut microbiome is important for healthy brain function, as it is linked to the production of neurotransmitters and hormones that regulate mood and behavior.

Keywords: Psychobiotics Probiotics Limosilactobacillus reuteri Alzheimer microbiota

LINC03052/ hsa-miR-361-5p/ CLEC1B CeRNA axis can be involved in the HCC by mediating in C-type lectin receptor signaling pathway (Research Paper)

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Introduction: Hepatocellular carcinoma (HCC) is one of the most common tumors in the world, with a high mortality rate and poor treatment outcomes due to an unclear molecular foundation. It appears that gene expression is important in the pathogenesis of the disease. Circular RNAs (circRNAs) can act as competitive endogenous RNAs (ceRNAs) to regulate gene expression in many malignancies by interacting with microRNAs (miRNAs). However, the potential pathogenic functions of the ceRNA network in HCC pathogenesis are unknown. This study has employed bioinformatics analysis to detect novel biomarkers for prognostic and diagnostic targets.

Methods: We used DEGs (Differentially expressed genes) between cirrhotic Non-malignant liver tissue and tumor tissue to analyze gene expression profiles and find genes of importance in the development of hepatocellular carcinoma. Microarray data(GSE54236) was obtained from NCBI Gene Expression Omnibus (GEO). this data was analyzed by GEO2R and genes with significant differential expressions (logFC <-3 and adjusted p-value <0.05) were selected. The miRWalk was used to analyze miRNA–mRNA interactions. To find proper lncRNAs, miRNAs were searched in LncBase v.3 and several lncRNAs were found. For more, to confirm that the lncRNAs are highly significant in hepatocellular carcinoma, the lnCAR database was employed. Using GEPIA2 for validation of mRNA, and using ENCORI for validation of miRNA and lncRNA. Moreover, The Pathway enrichment analysis was carried out using KEGG.

Results: GEO2R analysis shows that CLEC1B gene to be meaningfully downregulated in Liver Hepatocellular Carcinoma (LIHC) (logFC=-3.4951, adj. P value =4.40E-12). CLEC1B gene was validated by the GEPIA2 database. Analysis of probable mRNA-miRNA interaction by miRwalk and ENCORI showed that hsa-miR-361-5p has significant interaction with CLEC1B mRNA in the 3’ end. By entering this miRNA in Lncbase v.3 and validating the interaction in ENCORI, it was revealed that LINC03052 (lncRNA) had a significant correlation with the mRNA. Additionally, to ensure that lncRNA is a

high expression in hepatocellular carcinoma, the lnCAR database was employed, and the level of expression was 2.5191. Moreover, Kyoto Encyclopedia of Genes and Genomes(Kegg) database confirmed that CLEC1B is a component of C-type lectin receptor signaling pathway which has a critical function in anti-tumor immune responses.

Conclusion: Current study reveals that, there might be a CeRNA network between CLEC1B, hsa-miR-361-5p, and LINC03052. The CeRNA network and signaling pathway increase the possibility that CLEC1B is a reliable biomarker for diagnostic and prognostic targets.

Keywords: Hepatocellular Carcinoma, CeRNA network, Prognostic biomarker, Integrated bioinformatic analysis

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Liposome-Loaded Hydrogels: Promising Biomaterials for Regenerative Medicine and Cancer Treatment (Review)

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Introduction: Liposomes are known as small artificial vesicles that can be prepared from cholesterol and natural non-toxic phospholipids. Regarding, their advantages including hydrophobic and hydrophilic character (besides biocompatibility), liposomes are well known in nanomedicine and considered as a promising option for drug delivery. Considering the very important role of drug delivery in tissue engineering and the undeniable role of sustained drug release in cancer treatment, liposomes have found many applications in tissue engineering and cancer treatment. On the other hand, considering the advantages of hydrogels such as biocompatibility, sustained release and structural diversity, hydrogels loaded with liposomes seem to be a suitable option for use in tissue engineering and cancer treatment.

Methods: In this review, PubMed, ISI Web of Science, Google scholar and SCOPUS databases were searched for studies published up to September 2023 related to “Liposome-Loaded Hydrogels: Promising Biomaterials for Regenerative Medicine and Cancer Treatment” were addressed.

Results: Studies demonstrated that liposome-loaded hydrogels have very promising results in wound healing, bone regeneration, targeted release of cancer drugs, and even improved immunotherapy. Most of these results are due to the reduction of toxicity caused by the local and targeted release of the drug, as well as the cell adhesion and biocompatibility of the hydrogel.

Conclusion: The use of liposome-containing hydrogels can provide smart systems for targeted cancer treatment and tissue regeneration.

Keywords: Liposomes, Hydrogels, Drug Delivery, Regenerative Medicine, Cancer Treatment.

Liposomes carrying hydrophilic and hydrophobic drugs (Research Paper)

hossein ameri shahrabi,[1,*]

1. Education

Introduction: The field of drug delivery has witnessed remarkable advancements in recent years, aiming to enhance the efficacy and safety of therapeutic agents. Among the various drug delivery systems, liposomes have emerged as versatile carriers due to their ability to encapsulate both hydrophilic and hydrophobic drugs. Liposomes are spherical vesicles composed of lipid bilayers that closely resemble cell membranes, making them an ideal choice for drug delivery. This article explores the encapsulation and delivery of hydrophilic and hydrophobic drugs using liposomes, highlighting their potential in improving drug bioavailability and minimizing side effects.

Methods: Liposome Preparation: Lipid composition selection: We carefully selected lipids to form liposomal bilayers, considering factors like biocompatibility and stability. Liposome preparation methods: We employed several techniques, including thin-film hydration, sonication, and extrusion, to create liposomes of varying sizes and characteristics. Encapsulation of hydrophilic drugs: We loaded hydrophilic drugs into the liposome aqueous core using the hydration method. Encapsulation of hydrophobic drugs: Hydrophobic drugs were incorporated into the lipid bilayer during liposome formation. Characterization: Size and morphology analysis: We used dynamic light scattering (DLS) and transmission electron microscopy (TEM) to determine liposome size and shape. Drug encapsulation efficiency: High-performance liquid chromatography (HPLC) and UV spectroscopy were employed to quantify drug loading and encapsulation efficiency. Stability assessment: Liposome stability was evaluated under various conditions such as temperature, pH, and serum. In Vitro Release Studies: Release profiles of hydrophilic and hydrophobic drugs were investigated under simulated physiological conditions to assess drug release kinetics from liposomes. In Vivo Studies: Animal studies were conducted to evaluate the pharmacokinetics and tissue distribution of liposome-encapsulated drugs. Toxicity assessments: We monitored any signs of toxicity or adverse effects associated with liposomal drug delivery.

Results: Our study demonstrates the potential of liposomes as effective carriers for both hydrophilic and hydrophobic drugs. The versatility of

liposomes in accommodating diverse drug types makes them a promising candidate for drug delivery applications. Key findings from our research include: Enhanced Drug Bioavailability: Liposomes can significantly improve drug solubility and stability, leading to increased bioavailability of both hydrophilic and hydrophobic drugs. Controlled Release: Liposomes can be tailored to release drugs in a controlled manner, prolonging therapeutic effects and reducing the frequency of dosing. Minimized Side Effects: By encapsulating hydrophobic drugs within liposomes, we observed a reduction in off-target effects and enhanced drug safety. Biocompatibility and Stability: Liposomes displayed good biocompatibility and stability, making them suitable for further development and clinical applications. In conclusion, liposomes represent a promising avenue for drug delivery, offering solutions to challenges associated with hydrophilic and hydrophobic drugs. Future research should focus on optimizing liposomal formulations and exploring their potential for specific disease treatments, bringing us closer to more effective and safer drug delivery strategies.

Conclusion: Our study demonstrates the potential of liposomes as effective carriers for both hydrophilic and hydrophobic drugs. The versatility of liposomes in accommodating diverse drug types makes them a promising candidate for drug delivery applications. Key findings from our research include: Enhanced Drug Bioavailability: Liposomes can significantly improve drug solubility and stability, leading to increased bioavailability of both hydrophilic and hydrophobic drugs. Controlled Release: Liposomes can be tailored to release drugs in a controlled manner, prolonging therapeutic effects and reducing the frequency of dosing. Minimized Side Effects: By encapsulating hydrophobic drugs within liposomes, we observed a reduction in off-target effects and enhanced drug safety. Biocompatibility and Stability: Liposomes displayed good biocompatibility and stability, making them suitable for further development and clinical applications. In conclusion, liposomes represent a promising avenue for drug delivery, offering solutions to challenges associated with hydrophilic and hydrophobic drugs. Future research should focus on optimizing liposomal formulations and exploring their potential for specific disease treatments, bringing us closer to more effective and safer drug delivery strategies.

Keywords: Liposomes carrying hydrophilic and hydrophobic drugs-hydrophilic liposomes

lncRNAs Participate in Epigenetic Regulation in Brest Cancer (Review)

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Introduction: The most frequent malignancy in women and the primary cause of cancer-related deaths globally is breast cancer (BC). Although there have been substantial improvements in clinical therapy, mortality has continued to rise due to the prevalence of breast cancer. Originally, it was believed that long non-coding RNAs (lncRNAs) were just the genome's background noise of transcripts and had no biological purpose. The purpose of lncRNAs has recently come under increased scrutiny. By controlling gene transcription and post-transcriptional processing, studies increasingly demonstrate that lncRNAs have a role in a variety of cellular physiological processes, including proliferation, differentiation, migration, and death. This research looked into how lncRNAs regulate epigenetic changes in breast cancer.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Epigenetic regulation does not alter the DNA sequence to cause heritable changes in gene expression, including DNA methylation, histone modification, genome imprinting, and random chromosome inactivation. Some important functions of lncRNAs are related to the epigenetic control of specific target genes For example, lncRNAs basal-like breast cancer-associated transcript (BLAT1), BCLIN25, and H91 can regulate DNA methylation to participate in tumorigenesis.9) Han found that BLAT1 expression is regulated at the epigenetic level by decreasing DNA methylation of CpG islands in the promoter. Patients with BLAT1-hypomethylated tumors have lower overall survival (OS). The increased BLAT1 expression with hypomethylation at CpG sites may contribute to the aggressive phenotype of breast cancer.57 BCLIN25 increases ERBB2 expression by enhancing CpG methylation of the miR-125b promoter, leading to the downregulation of miR-125b and promoting the occurrence of breast cancer. Also, the lncRNA 91H of the H19/IGF2 locus is transcribed in the H19 antisense orientation. In breast cancer, 91H lncRNA prevents DNA methylation of the maternal allele at the H19/IGF2 locus, thereby increasing the aggressive phenotype of breast cancer cells. In addition, lncRNA also inhibits gene transcription by recruiting histone modification or chromatin remodelling proteins.4 lncRNA HOX

transcript antisense RNA (HOTAIR) plays a critical role in chromatin dynamics through the interaction with histone modifiers resulting in transcriptional gene silencing.59 HOTAIR is participated in the silencing of miR-205 by breaking the balance of histone modification between histone H3 at lysine 4 methylation (H3K4me3) and H3K27me3 on the miR-205 promoter to regulate cyclin J (CCNJ) expression.

Conclusion: Breast tumour formation, diagnosis, and treatment, as well as patient prognosis, are all significantly influenced by lncRNAs. A few lncRNAs have currently had their function mechanisms thoroughly examined in exploratory study. Most lncRNAs' underlying functional mechanisms in breast cancer are still poorly understood, though. The secondary structure of lncRNAs is more complex than that of mRNA, and it has been acknowledged that lncRNA expression is more strictly regulated than mRNA. A small portion of lncRNAs expresses polypeptide products, much like mRNA does. As a result, lncRNA function mechanisms are extremely complex. Since the number of lncRNA genes exceeds protein-coding genes, lncRNAs are more stable than mRNA, so they are more suitable. All in all, lncRNAs open a new door for clinical diagnosis and treatment of breast cancer.

Keywords: LncRNA, Epigenetic, Brest Cancer

Low Dose Effects of Green Synthesized Silver Nanoparticles on Amyloid β-induced neurotoxicity in rats (Research Paper)

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2. Department of Biology, Faculty of Sciences, University of Razi, Kermanshah, Iran

Introduction: The application of nanotechnology for treatment of Alzheimer's disease (AD), as a progressive cognitive disorder has become a striking topic in researches. One of the contributing factors in the pathophysiology of AD is the imbalance in redox state of neuronal cells. Human cells exposure to silver nanoparticles (SNPs) is inevitable due to broad use of them in food and drug industries. As well as, nowadays they are considered as an attractive therapeutic opportunity for human diseases. While numerous studies have demonstrated the toxicity of SNPs on neuronal cells, their anti-inflammatory, and restrictive effect on neurotoxicity have also been reported. Meanwhile, the green synthesis method (using plants' extracts) is a strategy to diminish the toxicity of SNPs.

Methods: In this regard, we assessed the effects of green synthesis of SNPs via leaf aqueous extract of M. communis plant in an animal model of cognitive decline. Induction of cognitive impairment was performed by intracerebroventricular (ICV) injection of amyloid beta (Aβ) in male rats. The 0.1 ppm of Green-SNPs were prepared in deionized water and dispersed with an ultrasonic shaker for 20 min before each injection. Animals were dedicated to 5 groups by chance (n=10): 1) Intact group: remained intact during the experiments; 2) Sham group received intra-ICV injection of saline; 3) Green-SNPs group received intra-ICV injection of Green-SNPs; 4) Aβ group which received intra-ICV injection of Aβ (20 µg/10µl); 5) Aβ+Green-SNPs group which received Green-SNPs, one hour after intra-ICV injection of Aβ. We evaluated the behavioral indices using y maze, novel object recognition, elevated plus maze and passive avoidance memory tests. The redox status assessment was performed via malondialdehyde and superoxide dismutase activity analysis in hippocampus tissue.

Results: We observed a cognitive impairment, anxiety behavior, an increase in lipid peroxidation and a reduction in superoxide dismutase activity in the Aβ -injected rats. Administration of Green- SNPs (at doses the 0.1 ppm)

significantly improved behavioral indices. It also, decreased lipid peroxidation and increased superoxide dismutase activity.

Conclusion: Current findings suggested that potential ability of sub-toxic doses of Green-SNPs on relieving memory impairment in an animal model of AD. The observed positive role of Green-SNPs on behavioral indices may be due to the antioxidative effects of Green-SNPs. Understanding the biological effects of Green-SNPs, can be used to make future safe classes of SNPs or may pave the way to new therapeutic approaches in brain diseases.

Keywords: Green silver nano particles, Alzheimer's disease, Hippocampus, Redox status.

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Low frequency of differentially methylated genes among differentially expressed genes and their positive or negative correlations in colon adenocarcinoma (Research Paper)

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Introduction: DNA methylation is a regulatory mechanism of gene expression. Disruption in gene expression and DNA methylation are promising cancer biomarkers and therapeutic targets for cancer therapy. The aim of this study was to determine the consistent or conflicting patterns between gene expression and DNA methylation in colon adenocarcinoma (COAD).

Methods: Differentially expressed genes (DEGs) ($|log2FC| \geq 1$ and p-value < 0.001) and differentially methylated genes ($|\Delta\beta| \geq 0.02$ and p-value < 0.001) in COAD were retrieved from the public OncoDB database. Enrichr database was used for the functional evaluation of DEGs.

Results: We identified 1414 downregulated and 1402 upregulated genes in COAD. The chemokine signaling pathway and cell cycle were the most significantly enriched pathways of downregulated and overexpressed genes, respectively. 1136 genes showed differential methylation in tumor compared to normal tissues; only 107 of them were among the DEGs. In 55 genes, hyper-methylation was accompanied by a decrease in expression; and 15 overexpressed genes showed hypo-methylated promoter. However, 14 genes showed decreased expression when their promoter hypo-methylated; additionally, 10 upregulated genes showed hyper-methylated promoter.

Conclusion: In conclusion, alteration of DNA methylation did not contribute to COAD development exclusively via a direct effect on gene expression. In addition, not all DEGs undergo a change in DNA methylation level, and correlations between methylation level and gene expression could be positive or negative. Other factors such as the location of DNA methylation, non-coding variants, and context of the tumor microenvironment can be involved in gene expression regulation.

Keywords: Differentially expressed genes, DNA methylation, Colon adenocarcinoma, OncoDB database

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Low molecular weight b-FGF supplementation causes the HT29 colon cancer cell line more susceptible to apoptosis resistance (Research Paper)

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4. Infectious and Tropical Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: The basic fibroblast growth factor (bFGF) is a signalling molecule involved in tissue regeneration, cell proliferation, and morphogenesis. Some studies claim that bFGF is necessary for the development, distribution, and development of tumours. However, other studies have revealed that bFGF causes cancer cells to undergo apoptosis. This investigation aimed to investigate bFGF's impact on the development and survival of the HT29 colorectal cell line.

Methods: HT29 cells were treated with 25 ng/mL of 18 KD bFGF for 48 h. Cell viability was determined using an MTT assay. A clonogenic assay was performed using crystal violet staining. The gene expression was investigated using the Real-Time PCR method

Results: Different concentrations of bFGF had no toxic effect on HT29 cells ($P > 0.05$). The viability of the bFGF-treated cells was higher than control cells. However, the difference was not significant ($P > 0.05$). The ability of clonogenicity in the bFGF-treated group was not significantly different from the control group ($P = 0.1039$). The expression of Bax in the bFGF-treated group showed a significant decrease compared to the control group ($P = 0.0046$). However, the expression of BCl2 was significantly increased in the bFGF-treated group ($P = 0.0011$). The bFGF therapy decreased the expression of Caspase3 while increasing the expression of CyclinD1 and Survivin even though they were not statistically significant ($P = 0.1899$, 0.1204 and 0.1586 respectively).

Conclusion: The bFGF can be considered an inducer of proliferation that resists apoptosis in the HT29 colorectal cell line.

Keywords: Colorectal Cancer, bFGF, apoptosis, HT29 cell line

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Conclusion: The bFGF can be considered as an inducer of proliferation that provides resistance to apoptosis in the HT29 colorectal cell line.

Keywords: Colorectal Cancer, bFGF, apoptosis, HT29 cell line

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Low-power sonication can reduce the size of SHED-MSCs-derived exosomes (Research Paper)

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Introduction: Exosomes isolated under laboratory conditions are prone to aggregation, which causes problems in identifying their characteristics such as particle size and concentration. This study investigated the effects of sonication at different time periods and then analyzed the properties of SHED-MSCs-derived exosomes using DLS and AFM techniques.

Methods: After incubating the SHED-MSCs in a serum-free medium, the supernatant was collected and SHED-MSCs-Exo was isolated using the Exocib Exosome Isolation Kit (Cibbiotech, Tehran, Iran) according to the manufacturer's protocol. The extracted exosomes were divided into three groups: sonication, 5 min sonication, and 10 min sonication.

Results: DLS and AFM analyses of the three groups of exosomes show that the size of exosomes before sonication is in the range of 100-1000 nm, while after 5 min of sonication, their size is in two ranges or two peaks of 10-100 nm and 100-1000 nm. In the third group, after 10 minutes of sonication, all exosomes were found to be between 10 - 100 nm in size.

Conclusion: Low-power sonication has been widely used to dissociate aggregates of isolated exosomes prior to analysis. This technique separates particles by vibrations in a suspension.

Keywords: SHED-MSCs; Exosomes; Sonication; Particles

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Malaria disease, treatment and vaccination review article (Review)

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Introduction: Malaria is an infectious and contagious disease caused by a protozoan of the genus Plasmodium in tropical and subtropical regions. The symptoms of this disease are severe fever and chills and physical symptoms similar to the flu. Plasmodium is transmitted to humans by the bite of an infected female Anopheles mosquito, and it has several species, but the most common types are Plasmodium falciparum and Plasmodium vivax. Plasmodium falciparum is the most deadly malaria parasite and the most common parasite in the African continent.

Methods: A severe decrease in vitamin E is observed in patients with severe malaria. A decrease in the level of vitamin E in patients with malaria may indicate an increase in the need for increased destruction or an increase in the use of vitamin E during malaria infection, since the Plasmodium parasite affects red blood cells. In malaria patients, the cause of vitamin E deficiency may be its transmission. to the membrane of red blood cells to fight the increase of oxidative stress during the acute phase of Plasmodium infection. Vitamin E can protect the membrane of red blood cells against oxidative stress. In malaria disease, children and pregnant women are the most dangerous groups.

Results: Widespread chloroclin resistance and pirimethamine sulfadoxine resistance are increasingly recognized in Africa. Currently, the only malaria vaccine is RTS, which cannot be widely used due to its low efficiency. Consumption of antioxidant vitamin E and foods rich in vitamin E are recommended for the management of malaria patients. Therefore, the combination of antimalarial drugs with antioxidant agents can be a promising approach to increase the management and control of malaria

Conclusion: Malaria especially during pregnancy may lead to maternal death, miscarriage or stillbirth. Malaria disrupts the function of the placenta, especially in early pregnancies, and may even be transmitted from the mother to the fetus. The number of malaria patients is increasing with global warming. And most of the concern is due to the increase in mortality due to the increase

in malaria drug resistance. Plasmodium falciparum is now resistant to almost all antimalarial drugs.

Keywords: Malaria, VitamiE,Vivax,falsiparom,plasmodium

Marfan; A syndrome with specific characteristics to the individual (Review)

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Introduction: Marfan syndrome is a lifelong problem that occurs in 1 in 3000 to 5000 births. 50% chance that this syndrome will be inherited from parents; However, 25% of patients show variants of the disease that do not receive this mutation. In consecutive years, due to early diagnosis and medical research, the quality of life of these patients has increased.

Methods: In this article, Google Scholar data and its advanced search were used to find new articles between 2019 and 2023, and what is Marfan syndrome, diagnosis of Marfan syndrome, treatment of Marfan syndrome, effect of Marfan syndrome were searched.

Results: Marfan syndrome is an autosomal disorder in the connective tissue that is caused by a mutation in the FBN1 gene of chromosome 15. The FBN1 gene encodes a large glycoprotein called fibrin 1. These microscopic fibers have the role of structural support for tissues and organs. As we know, connective tissue is present throughout the body. This syndrome has the same frequency in men and women. signs The most significant problem in patients with Marfan syndrome is the defect of the aorta and heart valves, which may be life-threatening. Cataract, glaucoma, reduced vision and even blindness are the effects of this syndrome, so many patients wear glasses. Obesity is observed in elderly patients. This disease includes skeletal abnormalities such as lateral curvature of the spine, stretching of the face and upper body, thin and narrow body, deformity in the chest and arms and legs, hunchback and excessive bending of the joints. Other symptoms of this disease are irregular teeth, skin and lung problems, and disorders in the central nervous system. Also, psychologically, these patients have challenges in education, depression and anxiety, fatigue and sleep disorders. Part of this anxiety and depression is caused by dissatisfaction with the shape of the body, and this dissatisfaction is seen more in women than in men. Diagnosis: Despite the fatal problems caused by Marrfan syndrome, its timely diagnosis is very important. It is difficult to diagnose the disease due to the phenotypic diversity and the age-dependent nature of some of its symptoms, the high rate of spontaneous mutations, and the similarity of the symptoms of other

connective tissue diseases. First, we examine the patient in terms of personal symptoms and family history and complete physical examination and check them for the presence of symptoms. We identify these patients by performing echocardiography and measuring the diameter of the aorta from the heart point of view; also, the first degree relatives of the patient must undergo a physical examination. If there is a gene mutation, they should undergo genetic counseling and genetic tests, and only those who have a gene mutation should have their aorta examined. treatment: Drug treatments, for example, the use of Beta_Blocker drugs, which reduce cardiac symptoms; also, anticoagulant drugs such as warfarin, intravenous antibiotic therapy are used during cardiac surgery. Some patients with acute cardiac symptoms undergo emergency aortic surgery, which causes 20% death and 50-70% of them have a 10-year survival; if the non-emergency and elective surgery, the probability of death is 1-2%. In some cases, severe nystagmus requires surgery, and laser therapy is useful for retinal detachment. In general, this disease has no specific treatment; The prognosis of the disease, timely diagnosis and drug treatment should be increased to delay the progression of the disease.

Conclusion: Marfan syndrome is a disease that does not have specific symptoms, diagnosis and treatment, and the goal of treatment is to keep the disease process stable before it reaches acute stages and causes dangerous complications. It is better to increase the life expectancy of patients and to prevent abnormalities following the disease, to make a timely diagnosis based on clinical symptoms, to carry out specific genetic tests for patients and their first-degree dependents in order to prevent disability in the target society and mortality. caused by it to be prevented.

Keywords: Marfan syndrome, FBN1, connective tissue disease, genetic

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Mastalgia and decrease in sexual satisfaction: identification of sexual behaviors leading to sexual satisfaction and its predictors (Research Paper)

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Introduction: Introduction: Breasts are one of the most important sexual organs in women (1) and in some sources they are even considered as the second most important sexual organ in women, therefore the presence of pain and disturbance in the stimulation of the breasts can cause sexual dysfunction. 2) and it leads to sexual dysfunction, sexual behavior disorder (3) and a decrease in sexual satisfaction of people (4).

Methods: Materials and methods: This descriptive-analytical study was conducted on 204 women suffering from cyclic mastalgia who referred to four comprehensive health centers and clinics of Kausar Hospital in Qazvin city. First, cyclic mastalgia was diagnosed among people who met the criteria for entering the study using the objective pain line and breast pain table of the Cardiff Clinic, then the samples with cyclic mastalgia completed the sexual behavior questionnaires, Larson's sexual satisfaction evaluation index and researcher's demographic questionnaire. Linear regression model was used to determine the predictors of sexual behaviors leading to sexual satisfaction.

Results: Results:. The average age of the samples was 33.05 ± 6.145 years. The mean and standard deviation of sexual satisfaction among the participants was 80.93±14. an increase of one unit of sexual capacity behavior and sexual script, the level of sexual satisfaction increases by 0.47 and 0.25, respectively. For one unit increase in the number of sexual relations per week, the amount of sexual capacity increases by 0.19 and the sexual script increases by 0.31.

Conclusion: Conclusion: The results showed that among the four areas of sexual behavior (sexual capacity, sexual motivation, sexual performance, sexual script), only two areas of sexual capacity and sexual script are effective on the level of sexual satisfaction in women with cyclic mastalgia

Keywords: Keywords: mastodynia, sexual behavior, orgasm

Mature cystic teratoma (MCT) of the ovary (Review)

Arefeh Gholamhosseini,[1,*]

1.

Introduction: Mature cystic teratoma (MCT) of the ovary The most common tumor of ovarian germ cells in reproductive age is 10-20% of all ovarian neoplasms.-Dermoid cysts are usually clinically silent and are detected incidentally on medical imaging.They will be created in two ways: Congenital: it is the result of ectoderm implantation during embryogenesis, when the neural groove is closed.Acquired: due to surgery or trauma, which results in tissue implantation into the peritoneal cavity.A dermoid cyst is a single lesion, a subcutaneous nodule. It is pale in color or fleshy or pearly in color.It is covered by an epidermis-like epithelium that contains derivatives: mesoderm or endoderm or ectoderm, tissues such as skin, hair, or teeth.Most cystic teratomas are congenital. They occur in the second and third decades of life. They are usually unilateral and in 10% of cases they are bilateral and multicystic.The annual growth rate of dermoid cyst is 1.8 cm per year in premenopausal women. This cyst with a slow growth pattern often causes a delay in diagnosis.It has a 1-2% chance of becoming a malignant tumor and will cause ovarian cancer, which is the most common squamous cell carcinoma.

Methods: Giant cysts can be up to 30-40 cm in size ،They need to be removed due to pressure symptoms and risks of malignancy. Their treatment is done by full midline laparotomy and oophorectomy.Management of adult teratoma is influenced by malignancy, age of the patient, and the need for fertility preservation. Cyst removal is an effective treatment. Chemotherapy and drug therapy are considered targeted when any malignancy is present, or when it is combined with other ovarian cancers.Diagnosis will be done using sonography and MRI. MRI has 100% sensitivity.Surgery is the definitive treatment for dermoid cysts. This cyst may recur after surgery in 11% of cases, and re-surgery is required in 3% of cases. Surgery is performed either as ovary preservation or oophorectomy.

Results: Laparoscopy is a treatment that protects reproductive health and skin appearance. If the size of the cyst is less than 5 cm, this method is used. The fluid inside the cyst is aspirated by a vacuum aspirator using a Veress needle to prevent it from spilling into the lumen. In this method, the probability of cyst rupture is 100-15%. The risk of intraperitoneal rupture and peritonitis and adhesion is high.Laparotomy ،The main basis of surgery for large and

bilateral ruptured cysts. The risk of rupture is lower than laparoscopy.Mini laparotomy is minimally invasive. A small incision of 1-4 cm will be made. It is a way to preserve more ovarian tissue.Oophorectomy is performed in menopausal people , they have muscle pain in the lower body and the probability of malignancy is high.Dermoid cyst has a significant effect on fertility.The results showed that the removal of the ovarian dermoid cyst significantly reduces the ovarian reserve according to the size of the cyst itself. The presence or removal of the cyst has no effect on the result of IVF, but it reduces the ovarian reserve according to the AMH levels. Complications: twisting 16% _ Malignant degeneration 2% _ 1% infection _ Hemolytic anemia 1% _ Cyst rupture 1-2%.

Conclusion: The exact cause of dermoid cyst rupture is unknown ‹It is rare spontaneously because the cyst has a thick capsule ‹It usually occurs during pregnancy and may cause two complications: 1- Acute peritonitis and sudden release of the contents of the mass.2-Chronic granulomatous peritonitis (more common)which causes chronic leakage of contents and causes adhesion and ascites. Chemical peritonitis is a serious and rare complication during cyst removal with laparoscopy. To prevent it, they use abdominal lavage. It is successfully managed with a lot of pelvic washing and bowel rest. According to the research timely diagnosis and doctor's help are useful in improving the quality of life. Also, international cooperation is necessary for research and clinical trials in this field.

Keywords: Mature cystic teratoma Laparoscopy Fertility ovary peritonitis

Measuring the amount of catechin in plants Camellia sinensis L., Zizyphus jujuba MILLER with anti-diabetic properties (Research Paper)

Noushin Shakouri,[1,*]

1.

Introduction: Diabetes mellitus is an important metabolic disease that reduces the patient's quality of life due to acute and chronic complications and is formed by the failure of insulin secretion from the pancreas and the resistance of tissues to insulin and in the body affects the metabolism of fat, protein and carbohydrates. According to the Diabetes Atlas published by the International Diabetes Federation (IDF) of 2017, a total of 425 million people worldwide between the ages of 20-79 have diabetes and this figure will increase 48% and reach 629 million in 2045. The medical treatment of diabetes mellitus is based on hypoglycemic drugs and insulin. But nowadays due to the high cost and side effects of these drugs, there is an increasing interest in herbal and synthetic treatment methods as alternative treatments. To date, more than 1050 antidiabetic plants have been identified and about 300 active antidiabetic compounds have been isolated from them. Flavonoids constitute an important group of active antidiabetic compounds of plants. According to the studies, catechin is found as a flavonoid in many plants and fruits. Some of the antidiabetic effects of catechin can be summarized as follows: Strong antioxan effect, reducing the effect of alpha-amylase enzyme, preventing hemolysis of membrane of red blood cell, protecting pancreatic β cells from destruction. Increasing pump activity Ca+2-ATPase in the erythrocyte membrane. Increase insulin secretion and activity, Inhibition of activity Na+/H+ exchanger etc. In this study, Camellia sinensis L., Zizyphus jujuba MILLER, was collected for analysis.

Methods: In this paper, Camellia sinensis L., leaves, Zizyphus jujuba MILLER. fruit. Punica granatum L. fruit skin was collected for analysis with HPLC method. Firstly, the samples were dried and was obtained theirs ethanol extract in the form of a very fine powder with 80% ethanol , 5 grams of dried sample and 25 ml of ethanol by incubation method and then filtration operation. Catechin standard was purchased from (Sigma Aldrich) . The first catechin was injected into the device with concentrations of 0.02-0.03-0.04, 0.05, 0.06 mg/ml and was drawn its calibration curve. Then the samples were analyzed, 100 microliters of the sample extract was taken and concentrated to 1000 microliters under special conditions of the device : Catechin analyzes using with Agilent 1260 infinity HPLC by (Asih et al. ., 2022) method (It has been partially modified). Elavonoid standard and chemical materials used are

of analytical purity .The mobile phase consists of two solvent systems: [A: 0.1% formic acid); B: MeOH: ACN: Formic acid (9 : 1 : 0.1) Column name: Agilent zorbax 300SB C18 3.5 micrometer 4.6* 100 mm Flow rate is 1 mL/min, injection volume is 20µL. The column temperature was kept constant at 35°C throughout.

Results: The analysis results showed that there is catechin in all three samples, but its amount is significantly higher in Camellia sinensis L. leaf extract. In the table below, the amount of catechin in the samples is given in mg/ml. Cotechin amount of (mg/ml) in extract of sample Punica granatum L. Camellia sinensis L., Zizyphus jujuba MILLER are respectively 11/2824, 24/2668 and 6/8299.

Conclusion: In the findings of the analysis performed for the ethanol extract of three samples of Camellia sinensis L., leaves, Zizyphus jujuba MILLER. fruit. Punica granatum L. fruit skin confirm the presence of catechins in these samples. The amount of catechins in Camellia sinensis L.(green tea) is significantly higher than the other two samples. According to the proven effects of the flavonoid catechins in the treatment of diabetes, it can be concluded that in these three samples, especially green tea, there are antidiabetic effects caused by catechins and in the long term. These can be used as a treatment for diabetes. In future works, catechins can be isolated from these plants and added to foods to help balance blood sugar. These plants with anti-diabetic properties can be a source of herbal medicines. So, you can get natural medicines with reduced side effects.

Keywords: Diabetes Mellitus, Flavonoid, Catechin, , HPLC

Measuring the proton beam energy in different depths of Cancer Tumor (Review)

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Introduction: Radiation therapy (also called radiotherapy) is a cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors. Charged particles have a stable range in matter. They interact and produce ionization along their path in the material. When their velocity decreases, the ability to ionize and interact increases. Therefore, according to the particle energy, a peak is created in the depth of the target material. The highest depleted dose is called the Bragg peak. As we know, the accurate determination of Bragg curves can give us more precise results of proton energy in different depths of matter, so the study of Bragg curves is essential. There are three ways to determine Bragg curves in the target material: 1- Using the Monte Carlo simulation method: This method is achievable by using different nuclear codes. (such as MCNPX, GEANT4, etc.). 2-Using analytical calculation methods: Bragg curves are asymmetrical. One of the best presented analytical models for Bragg peaks, is the Bortfeld model. This model contains cylindrical parabolic functions and gamma rays. 3-Practical methods of dosimetry and detection: We use various types of detectors in this method.

Methods: The BL4S experiments take place in the T9 beam line of the CERN Proton Synchrotron (PS). The experimental area where the T9 beam line is located is one of the most intensively used. Thus, The CERN beam line is suitable for this measurement. Monte Carlo tool (GEANT4) is a simulation package for different geometries and transport of physical particles. In this research we used this tool to simulate a water phantom in the form of a cube. The energies of the proton beams are chosen so that the Bragg peaks cover the range between 8.2 and 12.9 cm. The energy range of the primary shots for 1 million protons is between 113-140 MeV. In order to ensure the accuracy of our simulation, we drew the Bragg peaks using Mathematica software in the same energy range. For a better review, we fitted the Bortfeld curve on the obtained curve from the GEANT4 simulation (for the energy of 119 MeV). Now we are looking for a practical Method to measure the deposited energy.

Results: we suggested a detector which is based on the operation of a type of transistor. This transistor is exposed to proton beams. Proton radiation to the negative n-type material of the detector increases the number of charge

carriers which leads to generation of current. This sensor consists of a 300 µm silicon layer. The n-type Si-chip is implanted with boron and phosphorus on the front and backside, respectively. Aluminum electrodes are then sintered to provide electrical contacts. Now we provided an idea to place this sensor in a circuit. In this circuit, for a better recognition of proton interactions with the sensor, we can increase the generated current by using an amplifier (NPN transistor). We consider three ways for this detection: 1.The current through the galvanometer 2.Luminous intensity in LED (light emission diodes) 3.LEDs with different colors which are produced by different currents Protons with high energy can damage the detector. Consequently, we also put a one-millimeter aluminum sheets as protective layers. We have to put number of shields in the path of the beam line, based on the detector's depth in water phantom. The energy loss of protons in these sheets is precisely determined. In water phantom the closer we get to the Bragg peak, the more interaction The proton would have. As a result, we would have higher current along the track. The highest interaction would be at the Bragg peak's location and afterwards the generated current highly decreases. The sensor can be designed in very small sizes due to the used technology. Thanks to this, the whole target screen can interact with protons in any depth. This function is used to calibrate the proton beams.

Conclusion: our scientific proposal underscores the vital importance of proton therapy in the treatment of cancer. Proton therapy offers a promising approach to deliver precise doses of radiation to cancer cells while minimizing damage to healthy tissues. The accurate determination of Bragg curves, as demonstrated in our research, plays a crucial role in optimizing proton therapy's effectiveness. By utilizing advanced methods such as Monte Carlo simulations and practical detectors, we have made significant strides in improving the precision and reliability of proton therapy. Our proposed detector, based on a type of transistor, offers a practical solution for measuring deposited energy during proton therapy, enabling better control and monitoring of the treatment process. Furthermore, the use of shields and the precise energy loss calculations for protons in various materials, as outlined in our proposal, enhance the safety and accuracy of proton therapy. This innovative approach allows for the calibration of proton beams and ensures that the highest interaction occurs precisely at the Bragg peak's location, leading to more effective cancer treatment. In conclusion, our research contributes to the ongoing advancement of proton therapy, highlighting its potential to revolutionize cancer treatment by delivering highly targeted radiation therapy and minimizing side effects on healthy tissues. Proton therapy holds great promise in improving the lives of cancer patients, and our work brings us one step closer to realizing that potential.

Keywords: Proton therapy, Bragg peak, Monte Carlo simulation, Detector technology, Radiation dosimetry

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Medicinal plants used against Echinococcus granulosus (Review)

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Introduction: A zoonotic disease, cystic echinococcosis (CE), is caused by the larval stage of Echinococcus granulosus. There are still many countries around the world where it is a significant public health and economic issue. Depending on the location and stage of the cyst, CE poses a severe health threat to its intermediate hosts, such as humans, sheep, goats, and cattle, as it grows in the viscera. E. granulosus infections typically occur in vital organs like the brain, liver, and lungs. The disease is treated according to the location, size, and stage of the cysts. To date, CE is treated with four methods: surgery (the only option until the 1980s), puncture aspiration injection and re-aspiration (PAIR), chemotherapy using synthetic drugs such as benzimidazole compounds, and watch-and-wait for clinically inactive and silent cysts. There are, however, some significant limitations to these treatment methods. Various medicinal plants and their components are studied for their in vitro/in vivo scolicidal effectiveness against Echinococcus granulosus in this study.

Methods: ScienceDirect, Google Scholar, Scopus, and PubMed are universally recognized databases for retrieving published data (from 2000 to 2020). An evaluation of the published literature was carried out in order to identify the medicinal plants and compounds that had scolicidal activity against E. granulosus. The keywords used to search the database were "natural products against protoscoleces," "scolicidal agents," "scolicidal activities of plants in vitro or in vivo," and "medicinal plants employed against E. granulosus." 700 studies were funded. 670 abstracts were omitted, and 30 full texts were read. In total, 15 relevant articles with complete abstracts were included in the study.

Results: The most commonly used anti-Echinococcus herbs were Zataria multiflora, Berberis vulgaris, Nigella sativa, Allium sativum, and Zingiber officinale (ginger). Leaves are also widely used. A number of active compounds have been identified, including carvacrol, thymol, menthol, genistein, berberine, thymoquinone, gallic acid, and ampelopsin. All seven

compounds were tested in vitro for their effectiveness against protoscoleces, but only two (carvacrol and thymol) were studied in vivo. While the mechanisms by which phenolic monoterpenes affect protoscoleces are not fully understood, research on other eukaryotic cells shows that they have a significant effect on the plasma membranes and mitochondria. Through their penetration, they damage the lipid bilayer and alter cell permeability. The result is an increase in ion leakage and a decrease in membrane electric potential. Plasma membrane electric potential changes may result in leakages of proteins, amino acids, ATP, and electrolytes, especially calcium and potassium. This leads to membrane damage and cell death. Further, molecular changes within the mitochondrial membrane result in leaked radicals, proteins, calcium, and cytochrome C, leading to apoptosis.

Conclusion: Researchers have developed a great deal of interest in a variety of plant extracts, as well as essential oils, for the purpose of finding compounds with high scolicidal efficacy, which can be combined with or used in place of synthetic medications for CE treatment, both when combined with other compounds and on their own.

Keywords: Medicinal plants, Echinococcus granulosus, Hydatidosis

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Menopause and its physiological changes in women's body review articles (Review)

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Introduction: Introduction: Menopause is a physiological event in the life of women that usually occurs in middle age and at the age of 45 to 55 years, which indicates the permanent cessation of ovarian function and ultimately leads to the end of reproductive capacity and fertility. Menopause is a natural and gradual transition between active and inactive ovarian functions that lasts several years in women's lives and includes changes in the body and mind. During menopause, women enter a phase of estrogen deficiency, which accelerates the aging process. They are more likely to suffer from arthritis compared to men, and the prevalence of this disease in women during menopause increases significantly. It also indicates a period of There are significant fluctuations in the concentration of sex hormones. Sex hormones include estrogen, progesterone, testosterone and anti-Müllerian hormone, which have inflammatory effects and play a role in both neuroprotection and neurodegeneration.

Methods: Material methods: Compared to men, women face unique risks such as dementia, depression, MS, etc. due to hormonal and brain changes during menopause. Women are significantly more prone to depression than men. Fluctuations in ovarian estrogen hormone levels are closely related to women's well-being. In addition, the role of this hormone in modulating brain function and activity, serotonin neurotransmission, as well as induction of inflammatory response has been discussed. Yoga plays a significant role in women's health. Yoga is a way for the physical, mental, social and spiritual well-being of humanity without any other side effects. Now a days semi dangerous busy life, no body has time to take care of itself, especially women. This affects the health of women in middle or late middle age.

Results: Result : Therefore, the findings on whether the decline in estrogen levels after menopause is a risk factor for dementia in women are still debated. Also, about the prevention of dementia in postmenopausal women, both primary prevention (primarily drug intervention) and secondary prevention (mainly diet and weight loss) continue.

Conclusion: Conclusion: The most common problems such as menopause, stress, depression, lack of sleep, cardiovascular disorders, etc. Yoga is the best way to overcome these problems and have a healthy and happy life in this society. Worldwide, dementia is becoming one of the greatest challenges to public health. Many premenopausal symptoms such as headaches, depression, insomnia and cognitive decline are neurological in nature. Therefore, it is very important to study the brain before menopause. The findings suggest that the risk of dementia in women is partly related to hormonal changes during menopause.

Keywords: Menopause - Dementia - Depression - Estrogen hormone - Yoga

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Mental health of the elderly in the face of natural disasters (Review)

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Introduction: Human confrontation and conflict with natural phenomena and unexpected events is one of the major problems of human societies and has a history as long as the history of human life. Despite scientific and technological advances, people have not yet been able to master these disasters and reduce the damages caused by them and the death toll. In this article, the researchers have investigated the ways to prevent social psychological consequences caused by the occurrence of natural disasters, which directly affect the maintenance of the system and the health of the society.

Methods: This is a research study of review and library type, and by studying reliable websites, articles, theses, and reliable books, which investigated issues related to social psychological consequences caused by natural disasters in the elderly.

Results: After disasters, people are exposed to many stressful factors. The main factors are: 1- types of physical injuries that cause pain and discomfort. 2- Not having a safe place for comfort and rest. 3- Encountering heartbreaking scenes; All these factors cause a lot of psychological pressure on people. The stress placed on a person during disasters is very debilitating and can knock anyone down.With the occurrence of severe mental stress caused by the disaster, reactions and symptoms occur in people and if not handled, they can lead to chronic mental disorders. Some of the symptoms and nervous reactions are: 1- Anger 2- Anxiety 3- Disappointment 4- Fear 5- Frustration 6- Sadness About 2 to 3 months after the incident, the stage of facing the reality begins. At this stage, the survivors realize the depth of the disaster and the irreparability of a large amount of damages. Vague physical complaints without physical illness are the effects of natural disasters. Symptoms and psychological reactions of people in disasters may continue even after a long time has passed. If these symptoms are severe or persistent and cause harassment to a person, it requires specialized intervention and psycho-social support.

Conclusion: The findings of this research show that the survivors need more psychological support, because they may lose their spirit again and become depressed and anxious and feel very lonely. It is very important to create a spirit of hope and trust and accuracy in the fair distribution of facilities at this stage. If there is no timely diagnosis and no recognition of the symptoms of any of the mentioned disorders, the disease will stabilize in the survivors and its treatment will be difficult. Timely intervention in accidents and disasters reduces its psychological and social effects, and the existence of previous preparation for the damage caused plays a protective role against stress, therefore, it is recommended to carry out necessary training programs for different sections of the society and health care workers.

Keywords: Aging, mental health, stress, natural disasters, psychological support.

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Mesenchymal steam cell exosomes for cancer therapy; insights and challenges (Review)

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Introduction: One of the recent cancer treatment methods that has gained significant attention in recent years is therapy through mesenchymal stem cells. Mesenchymal stem cells can serve as a suitable therapeutic approach for eliminating cancer by carrying drugs through exosomes, facilitating easier entry into the tumor microenvironment, and establishing communication with cancer cells.

Methods: This study was conducted on the subject of the role of mesenchymal stem cell for cancer therapy, by collecting content from Science Direct, Springer, Google Scholar, and PubMed sites.

Results: The results of various studies have shown that destroying the vascularization of cancer cells before complete cessation of the cancer cell cycle can lead to further growth of cancer cells. This is because they no longer face hindrance and can even thrive in low-oxygen environments. Mesenchymal stem cells, by utilizing the constructed vasculature of cancer cells as a gateway to reach the innermost regions of the tumor microenvironment and delivering drug-loaded exosomes, which in this case have higher toxicity towards cancer cells, can be a more focused area of investigation. Further research into the vascularization of cancer cells and drug-loaded exosomes can receive more attention in cancer therapy.

Conclusion: In conclusion, various methods have been introduced and tested for cancer treatment, among which mesenchymal cells, with easy access to the tumor microenvironment and bidirectional interaction with cancer cells, can act like a double-edged sword.

Keywords: cancer, mesenchymal stem cells, toxicity.

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Meta-analysis of gene expression changes in MCF7 cell lines treated with EGCG and apigenin (Research Paper)

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Introduction: Breast cancer is the most common cancer type in females in the Western world. It is caused by a combination of genetic and environmental factors. The risk of developing breast cancer increases with age, family history, and certain lifestyle factors, such as obesity and smoking.

Methods: Microarray technology is a powerful tool that can be used to study gene expression profiles in breast cancer. This can help researchers to identify genes that are differentially expressed in breast cancer and gain insights into the pathways and biological processes that are dysregulated in the disease.

Results: EGCG and apigenin are two naturally occurring compounds that have been shown to have anti-cancer properties. Previous studies have shown that EGCG and apigenin can induce changes in gene expression in cancer cells. However, the results of these studies have been inconsistent.

Conclusion: A meta-analysis of these studies was conducted to provide a more accurate assessment of the effects of EGCG and apigenin on gene expression in breast cancer cells. The results showed that both EGCG and apigenin can induce changes in gene expression in breast cancer cells, including genes involved in cell proliferation, apoptosis, and angiogenesis.

Keywords: Breast cancer, Gene expression, Meta-analyses, Apigenin, EGCG

Metformin sensitizes gastric cancer cells to chemotherapeutic agents via modulating Shh/Gli1 pathway (Research Paper)

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Introduction: Gastric cancer (GC) is a crucial cause of cancer-related death characterized by poor prognosis. Docetaxel and 5-fluorouracil (5-FU) are approved for the treatment of GC, but chemo-resistance limits the application of it for GC. Metformin, a popular anti-diabetic drug, has been proven to have potent anticancer effects on gastrointestinal cancers. In this study we investigated the roles of metformin in the chemo-sensitivity of GC cells through targeting Shh/Gli1 Pathway.

Methods: Drugs and reagents were purchased from Sigma-Aldrich. The drugs were dissolved in RPMI at the specified concentrations and stored in a 4°C refrigerator. The human AGS cell line purchased from the National Cell Bank of Iran (NCBI, Pasteur Institute, Tehran, Iran). The gastric cancer cells were cultivated in RPMI 1640 (Gibco) medium, which was supplemented with 10% fetal bovine serum (FBS, Gibco) and 100 U/mL penicillin-streptomycin. The cells were incubated in a humidified atmosphere containing 5% CO2. The anticancer effects of metfotmin, 5-FU, docetaxel, and their combination on the AGS gastric cancer cells were evaluated by clonogenic assay and DAPi staining. We used immunocytochemistry assay to assess the expression of the Shh protein. Then, the expression of Gli1, Gli2, and TWIST1 mRNA determined using real-time PCR in these cancerous cells. All data were analyzed using SPSS V.21 software (SPSS Inc., USA). The significant differences were determined using Student's t-test and one-way ANOVA followed by the Tukey post hoc comparison test ($P<0.05$).

Results: our results demonstrated that metformin increases the sensitivity of GC cells to chemotherapy by enhancing the apoptosis rite and inhibiting clony formation ($p<0.05$). The co-treatment of GC cells with metformin, 5-FU, and docetaxel attenuated the expression of Shh protein ($p<0.05$). We also found that the combination of metformin with docetaxel significantly down-regulated the mRNA levels of Gli1, Gli2, and TWIST1 in the AGS gastric cancer cell line compared to docetaxel alone ($p<0.05$).

Conclusion: Overall, our data strongly support an important role for metformin as an enhancer of the efficacy of chemotherapeutic agents against GC via modulating Shh/Gli1 biomarkers.

Keywords: gastric cancer, metformin, docetaxel, 5-fluorouracil, cancer biomarcers

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Microalgae as Hygiene Indicators of Potable Water: The tip of the iceberg (Research Paper)

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Introduction: Microalgae are ubiquitous organisms that found in all fresh water sources and possess some medical issue. Since some microalgae lead to neurotoxicity or other organ toxicities, the purification and clarification of potable water to delete these organisms would be a crucial step to prepare clean and disinfected fresh water. Despite chlorination of civil water, some of these organisms may be become resistant to common disinfection methods and lead to organ toxicities following chronic intake. The goal of this study was to identify the microalgae that found in the tap water of our laboratories that supplied by well water.

Methods: Tap water (2 ml) has been centrifuged at 5,000 rpm and the clear pellet has been harvested and smeared and observed under light microscope 40X. The images of isolated microalgae were identified using available literature and databases. The indices of taxonomy, morphology, and morphometry have been employed to identify isolated microalgae.

Results: Through laborious work, a myriad of Cryptophyta and Haptophyta spp. have been isolated from spatial and temporal samplings of tap water.

Conclusion: Since microalgae possess an array of bio-compounds with unknown pathobiological effects and they are resistant to common disinfection methods, more purification strategies, investigations, and policies are acknowledged to understand their medical importance.

Keywords: Microalgae, Indicator, Potable Water, Chlorination, Purification

MicroRNA (miRNA) in cancer (Review)

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Introduction: MicroRNAs (miRNAs) are small non coding regions in RNAs of 20–22 nucleotides, which play an important role in all biological pathways in multicellular organisms including mammals that regulate gene expression at the post transcriptional level. They play a critical role in various cellular processes, including cell development, differentiation, and proliferation. However, dysregulation of miRNA expression or function can contribute to the development and progression of cancer. In cancer, miRNAs can act as oncogenes or tumor suppressors, depending on their targets and cellular context. Oncogenic miRNAs, also known as oncomiRs, are upregulated in cancer and promote tumorigenesis by repressing tumor suppressor genes or promoting cancer-associated processes such as cell proliferation, invasion, and metastasis. On the other hand, tumor suppressor miRNAs are downregulated in cancer and help maintain genomic stability, inhibit tumor growth, and induce apoptosis. The dysregulation of miRNAs in cancer can occur through various mechanisms, including genetic alterations, epigenetic modifications, and aberrant processing or maturation. Changes in miRNA expression patterns have been observed in virtually all types of cancer, and specific miRNAs have been implicated in the development, progression, and response to therapy in various cancer types, including breast, lung, prostate, colon, and ovarian cancer. MiRNAs have also been investigated as biomarkers for cancer diagnosis, prognosis, and prediction of therapeutic response. Their small size, stability in different biological fluids, and tissue-specific expression patterns make them attractive candidates for cancer biomarker development. Additionally, the ability to modulate miRNA expression and function holds promise for the development of miRNA-based therapies for cancer treatment. In summary, microRNAs play a crucial role in cancer biology by regulating gene expression and cellular processes. Dysregulation of miRNA expression or function can contribute to tumorigenesis and progression, making miRNAs attractive targets for cancer diagnosis, prognosis, and therapy

Methods: 1. Identification of differentially expressed microRNAs: This method involves comparing the expression levels of microRNAs in cancer tissues with that of normal tissues using techniques like microarray analysis or next-generation sequencing. 2. Validation of differentially expressed microRNAs: Once differentially expressed microRNAs are identified, their expression

levels are validated in a larger cohort of cancer patients using quantitative PCR or fluorescence in situ hybridization (FISH). 3. Target prediction and pathway analysis: Bioinformatics tools are used to predict potential target genes of the differentially expressed microRNAs. Pathway analysis is then conducted to determine the biological pathways and processes affected by these target genes. 4. Animal models and xenograft assays: Animal models, such as transgenic mice or xenograft models, are used to study the impact of specific microRNAs on cancer development, progression, and response to therapy. 5. Functional rescue experiments: To establish the direct functional relevance of specific microRNAs, experiments involving the rescue of microRNA-mediated phenotypes are performed. This can involve the introduction of a synthetic microRNA mimic or the restoration of target gene expression in the presence of a cancer-associated microRNA. 6. Therapeutic targeting of microRNAs: Based on the findings from the above experiments, therapeutic strategies targeting specific microRNAs can be developed. This can involve the use of antisense oligonucleotides (anti-miRs) to inhibit the oncogenic microRNAs or the use of synthetic mimics to restore the function of tumor-suppressive microRNAs. 7. Biomarker development: Lastly, selected microRNAs may be evaluated as potential biomarkers for cancer diagnosis, prognosis, or prediction of therapeutic response. This can involve developing sensitive and specific assays for their detection in patient samples, such as serum or plasma

Results: Researchers are focusing on the examination of body fluids such as plasma, serum, urine and saliva to determine the circulating levels of miRNAs and to evaluate if they can be used as diagnostic, prognostic and predictive biomarkers in cancer. Such studies have attracted a great deal of attention because of minimally invasive processes to examine miRNA using qPCR. In the serum of prostate cancer patients, the expression levels of pre-selected oncogenic miR-26a, miR-195 and let-7i were shown to be up-regulated compared to those in individuals with benign prostate hyperplasia (BPH) . Similarly, the prognostic value of increased expression levels of circulating miR-141 and miR-375 correlating with low-risk through high-risk and from localized to metastatic prostate cancer was documented . The signature miRNAs, miR-28-3p, miR-30c, miR-92a, miR-140-5p, miR-451 and miR660 in the plasma were found to be deregulated 1–2 years prior to diagnosis of lung cancer and thus, indicated their use in prediction as well as diagnosis . miR-27b, miR-158a, miR-326 signature or miR-200c in the serum of colon cancer patients were found to be useful to identify metastatic tumors . The miR-125b and miR-155 levels in the serum of breast cancer patients were found to be useful for diagnosis, assessing chemotherapeutic response as well as in prognosis . Until recently, miRNA analyses were performed using qRT-PCR and microarray-based approaches. NGS is now emerging as a cost-effective

option while bioinformatics analyses are no longer a major problem for continued usage

Conclusion: So far, there have been significant scientific research findings indicating the utility of miRNAs as biomarkers for prediction, diagnosis and prognosis. Evidence is also emerging suggesting that inhibition of oncogenic miRNAs or substitution of tumor suppressive miRNAs could be used to develop novel treatment strategies. The extensive information thus far available in the peer-reviewed scientific publications has been extremely useful to provide guidance for further investigations. Comprehensive, carefully designed, multi-centered, retrospective and prospective studies involving large cohorts in the same and independent laboratories/clinics comparing and validating the data within a similar type of cancer are warranted. Besides, investigations using minimally invasive methods to collect blood, saliva and urine are extremely important for the development of reliable and cost-effective miRNA-based technology for routine use in the clinics for early cancer diagnosis/detection and therapeutic assessment/prognosis.

Keywords: cancer . miRNA . diagnosis . Involvement

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MicroRNAs in Cancer: Insights from Bioinformatics Analysis (Review)

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Introduction: Cancer research has entered a new era, driven by the integration of bioinformatics tools and multidisciplinary collaboration. This review synthesizes findings from four research papers, offering profound insights into the pivotal role of microRNAs in various cancer types.

Methods: Our journey begins with "Predicting Glioblastoma-Associated MicroRNAs Through Bioinformatics Analysis," showcasing the transformative power of bioinformatics in identifying dysregulated microRNAs as potential diagnostic markers and therapeutic targets in glioblastoma. These discoveries, extracted from comprehensive analysis of genomic and transcriptomic data, hold the potential to revolutionize glioblastoma research. Moving forward, our exploration encompasses "Exploring MicroRNAs in Oral Cancer," emphasizing the critical role of the PLAU gene in oral cancer development. Utilizing GEO2R software and DAVID database analysis, we pinpoint PLAU as a significant gene, while the miRWalk database illuminates hsa-let-7e-5p and hsa-let-7b-5p as associated microRNAs, illuminating new avenues for research and therapy. In our final endeavor, we navigate the intricate landscape of "MicroRNAs in Helicobacter pylori-Related Gastric Cancer." Here, we uncover the insidious link between this bacterium and gastric cancer. Our investigation identifies CCL20 as a potent gene, intimately intertwined with has-miR223p and has-miR225p microRNAs, providing profound insights into the pathogenesis of this malignancy.

Results: This comprehensive review underscores the critical significance of bioinformatics-driven research and interdisciplinary synergy in unraveling the molecular intricacies of cancer. Each study's meticulously identified genes and microRNAs shed brilliant light on their roles in cancer initiation and progression, offering an invaluable roadmap for future investigations.

Conclusion: The revelations encompassed within this review extend far beyond scientific discourse. They pave the way for improved cancer diagnostics, targeted therapies, and a brighter horizon in cancer management. As we harness the potential of microRNAs and embrace the crossroads of genetics, bioinformatics, and oncology, we stride confidently towards the international congress, bearing the torch of innovation in cancer research.

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Keywords: MicroRNAs, Cancer, Bioinformatics, Genetic Analysis,Database

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MIR497HG/hsa-miR-4766-3p/KRT31 CeRNA axis affects Skin Cutaneous Melanoma development by regulating Keratinization signaling pathway & Estrogen signaling pathway: integrated gene expression profiling and systems biology analyses (Research Paper)

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Introduction: Skin cutaneous melanoma (SKCM) is a highly lethal type of skin cancer with a significant global mortality rate. The identification of reliable prognostic biomarkers and potential therapeutic targets is crucial for improving melanoma treatment outcomes. Recent studies have demonstrated the critical involvement of long non-coding RNA (lncRNA) in the regulation of gene expression in various diseases and tumors. Consequently, investigating the role of lncRNAs in the progression and advancement of SKCM is of utmost importance (1). Defining a competitive endogenous RNA(CeRNA) network provides valuable biomarkers and boosts the treatment process. CeRna theory claims that RNAs compete for a limited number of miRNAs; this competition affects the regulation of the cell. In cancer, the relationship between the components of this network changes (compared to the normal condition) and provides valuable information about the disease and its stage.

Methods: To begin with, GSE160902 has been chosen from NCBI Gene Expression Omnibus (GEO) and was analyzed with GEO2R in order to find gene with significant Decrease in expression regulation. KRT31 gene was chosen and its downregulation in (SKCM) was validated by the ENCORI database(2)(3). Using KEGG pathway database and Reactom gene ontology and biology pathways were determined (4)(5). miRNA interacting with KRT31 was obtained from miRWalk database(6). LncRNAs that have interaction with miRNA were acquired from LncBase v.3 the interaction between miRNA/LncRNA and miRNA/KRT31 were validated by ENCORI co_Expression analysis. Finaliy Cytoscape 3.9.1 was used to visualize ceRNA network.

Results: Based on GSE160902, 104 up and down regulated gene were determined. KRT31 down regulated gene were selected among these ups and down which has a interaction in Keratinization signaling and Estrogen signaling pathway. Compared to control (LogFC: -2.6192) (adj.P.Val < 0.001). GEPIA2 and ENCORI expression analysis validates the expression analysis

results. Based on survival analysis the low expression of KRT31 has a significant positive correlation with the survival rate of SKCM cancer(HR:1.62 logrank p: 0.00079). hsa-miR-4766-3p miRNAs was extracted from miRWalk 3.0. In addition, MIR497HG LncRNA was sponged by these miRNA that was extracted from experimental and predictive DIANA LncBase v.2 modules. As a result, these miRNAs and lncRNAs can act as a ceRNA network which has an effect on KRT31 gene regulation.

Conclusion: In summary, this finding could be suggested novel interactions among lncRNA, mRNA, and miRNA (MIR497HG, KRT31, hsa-miR-4766-3p) for the candidate diagnostic and prognostic markers associated with SKCM by bioinformatics analysis. We believe that, without any severe negative side effects, this ceRNA network could be used as a potential tool for both preventative and adjuvant treatment techniques in SKCM patients.

Keywords: SKCM gene expression KRT31

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Modification of RNA N6 methyladenosine for cancer treatment (Review)

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Introduction: Cancer has become a serious threat to human health, but its treatment faces many obstacles. N6-methyladenosine (m6 A) is the most common internal modification of eukaryotic mRNA. It modulates immune cell activation and microenvironmental (TME) infiltration and thus may affect the efficacy of immunotherapy. Abnormal regulation of m6A changes is essential for tumorigenesis, progression, invasion, metastasis, and apoptosis of a malignant tumor. Methylation modification at the 6th nitrogen atom of adenine that is dynamic and reversible. m6A is regulated by methylases ("writers") and demethylases ("erasers") and recognized and processed by m6A-binding proteins ("readers"), which further regulate the transport, localization, translation, and degradation of m6A RNA. This increases the expression of an oncogene or decreases the expression of a tumor suppressor gene and may become a therapeutic target for the malignancies that are the subject of this review

Methods: For the subsequent systematic review, the necessary data were collected, where possible, using the keywords and MeSH (medical title) terms listed below, as well as cross-referencing key databases such as PubMed, Science Direct and ProQuest. Additionally, a manual search was performed using Google Scholar to increase the sensitivity of the search. The statistical survey population includes all contextual studies conducted between January 2018 and January 2023. After reviewing the relevant results and assessing the quality of the pieces of evidence, 14 articles in English were reviewed

Results: Intrinsic modification of m6A regulates tumor cell fate by targeting specific genes in different cancer types. m6A readers such as YTHDF1 etc. indicate that these reader proteins are primarily intended to alter protein-RNA interactions by altering m6A homologous binding to RNA-binding proteins and RNA secondary structure. For example, impairment of YTHDF1 in gastric cancer progression results progression and poor prognosis. m6A methyltransferase includes methyltransferase 3 (METTL3), METTL14, WTAP, etc. also known as writer. Its primary function is to catalyze the m6A modification of adenylate on mRNA. All of these methyltransferases play an important role in the formation of METTL3-METTL14 complexes in various cells and influence tumor cell proliferation and migration. The study discovered four small molecules that can increase the activity of this complex. The reversibility of m6A modifications is due to demethylases such as FTO, the first demethylase discovered. the founded about how modification of m6A regulates the antitumor functions of immune cells: m6A writer METTL3 and reader YTHDF2 enhance the antitumor immunity of natural killer cells METTL3 and YTHDF2. METTL3-mediated modification of m6A leads to the activation and maturation of dendritic cells and causes them to present new antigens and thus activate T cells. Reduction of METTL3 in CD4+ T cells disrupts cellular homeostasis and cell differentiation and negatively regulates STAT5 activation via IL -7/suppressor Signaling cytokines (SOCS). Reduction of METTL3 inhibits Treg cell function and stability by inhibiting IL-2/STAT5 signaling and promotes cytokine secretion by effector T cells. This leads to an increase in the antitumor immune response in TME. Therefore, targeted modifications of m6A should: 1) inhibit tumor cell growth directly, 2) increase the antitumor potential of immune cells, e.g. increasing cytotoxicity of CD8+ T cells and NK cells, 3) remodel TME by reprogramming M2 TAM into M1 TAM.

Conclusion: Gradually, m6A emerged as an important epigenetic modification with reversible properties, an enzyme system associated with the modification, and a role in various disease processes. It offers unlimited possibilities for later diagnosis and treatment of cancer. Writers can catalyze the installation of m6A onto RNA, while erasers can remove these changes. Finally, reader recognition of m6A methylation affects splicing, export, degradation, translation, and other biological processes of mRNA.m6A seems to act as a double-edged sword in cancer. Some genes can promote tumor growth when methylated, while others, if methylation is suppressed, can promote tumor growth. For example, in CRC, SOX2 has a cancer-promoting role via METTL3-catalyzed methylation, while in breast cancer, BNIP3 has a cancer-promoting role via FTO-catalyzed demethylation. It is expected that these modified m6A molecules will become powerful markers for early cancer diagnosis and prognosis as well as potential therapeutic targets, thus providing new insights for cancer diagnosis and treatment.

Keywords: N6-methyladenosine, m6A methylation, neoplasms therapeutics, cancer immunotherapy

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Molecular Docking Analysis of Chamazulene as COX-2 Potential Inhibitor (Research Paper)

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Introduction: In this research article, we investigated the interaction between Chamazulene and COX-2 protein. For this purpose, we used the molecular docking method. COX-2 inhibitors (coxibs) are a type of nonsteroidal anti-inflammatory drug (NSAID) that directly target cyclooxygenase-2, COX-2, an enzyme responsible for inflammation and pain. Targeting selectivity for COX-2 reduces the risk of peptic ulceration and is the main feature of celecoxib, rofecoxib, and other members of this drug class. in this paper, the interaction between ligand and target protein has been investigated on in-silico step using bioinformatics methods. According to the obtained results, Chamazulene compound have a good interaction with COX-2 protein.

Methods: In this study, at first, we used uniport website and PDB website to extract protein's 3D structure as pdb file. After this, we made the protein ready for the project by making changes using Chimera software. COX-2(5KIR) had two chains, so we decided to keep all chains because there are cavities between the chains. Also, by using this software, water molecules were removed from the protein and hydrogen molecules were added to its structure. After this changes, we used pubchem website and drugbank website to extract 3D Structure of drugs as sdf file. finally, everything is ready for the molecular docking process by using PyRx software. In this research, the blind docking method was used. Therefore, the defined grid box includes the entire two chains of the protein. At the end, we used molegro virtual docker to check the results of different models.

Results: according to the numbers, Chamazulene has suitable interaction with COX-2 protein. So, it's clear that our compound can be docked to COX-2 protein. the numbers of binding affinity are suitable. also, we have normal range of numbers on RMSD

Conclusion: Therefore, we conclude that Chamazulene has analgesic and anti-inflammatory properties. however, in this article we just worked on in-silico. to prove these conclusions, in-vitro and in-vivo steps should be done

Keywords: Chamazulene, MolecularDocking, COX-2, Protein, Bioinformatic

Molecular docking of Cannabinoids with GABA receptor subunit alpha (Research Paper)

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Introduction: Gamma-aminobutyric acid type A (GABAA) receptors play a crucial role in facilitating rapid synaptic inhibition within the brain. Recent advancements in technology have greatly improved our understanding of the distinct roles played by various GABAA receptor subunit classes and isoforms in normal brain function. Clinical drugs and general anesthetics target numerous GABAA receptors, with each combination of receptors mediating distinct physiological functions. Cannabidiol (CBD), a non-intoxicating component of cannabis, possesses anti-epileptic and anti-hyperalgesic properties. While some endogenous and synthetic cannabinoids interact with GABAA receptors, the mechanism of action of CBD requires further investigation .CBD, one of two main cannabinoids found in the cannabis plant, has various functional effects and can alleviate psychotic symptoms. Evidence suggests that CBD act as a positive allosteric modulator for all GABAA receptors containing α subunits.

Methods: Molecular docking was performed using AutoDock Tools to assess the binding affinity of the ligand CBD with the GABA receptor, demonstrating the ligand's ability to localize within GABA. The calculation of binding free energies and inhibition constants for the best-docked complex of the ligands and the protein was carried out using AutoDock 4.2. The protein's structure was initially determined using https://blast.ncbi.nlm.nih.gov, and the three-dimensional crystal structure of the protein was obtained through the website http://www.rcsb.org. Ligands were prepared by downloading their chemical composition in SDF format from https://pubchem.ncbi.nlm.nih.gov. Subsequently, their PDB structures were obtained and saved using http://www.cheminfo.org/Chemistry/Cheminformatics/FormatConverter/index.html.

Results: Molecular docking revealed the binding affinity of cannabinol (CBN) and cannabidiol (CBD) to the alpha 1 subunit of the GABA1 receptor, which is a key inhibitory neurotransmitter receptor in the mammalian brain. The results indicate that both cannabidiol (CBD) and cannabinol (CBN) have the potential to form complexes with the GABA receptor. The binding free energy for CBN is -4.87 kcal/mol, which is more negative than that for CBD (-4.27 kcal/mol), suggesting stronger binding for CBN. Additionally, the inhibitory constant (Ki)

for CBN is smaller than that for CBD, indicating that CBN possesses greater inhibitory potential. Consequently, CBN, with its more negative binding free energy and smaller Ki, is deemed a more suitable ligand for the GABA1 receptor.

Conclusion: The field of molecular docking, with its computational ability, has emerged as a powerful tool in predicting drug candidates for various diseases. This research has shed light on the significance of GABAA receptors in the central nervous system and their implications in neuropsychiatric disorders. GABAA receptors, with their diverse subunit compositions and roles, are key players in maintaining neural communication and homeostasis. Their modulation by compounds like cannabidiol (CBD) raises intriguing questions about the mechanisms underlying their therapeutic effects. As the understanding of GABAA receptors and cannabinoids deepens, new avenues for drug discovery and the treatment of neurological and psychiatric disorders may emerge

Keywords: GABA, molecular docking, CBD, drug, cannabinoid

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mRNA Vaccine Technology: a Novel Weapon in Treatment Infectious Diseases and Cancers (Review)

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Introduction: Infectious diseases and cancer have threatened human life, but with the progress of vaccines, practical approaches for preventing these diseases have become available. During recent decades, there has been comprehensive attention to RNA-based knowledge for developing therapeutic and prophylactic vaccines. mRNA vaccine technology can combat cancer and viral diseases due to efficacy, safety, and large-scale production advantages.

Methods: This study included peer-reviewed papers from Scopus, PubMed, Web of Science, and ScienceDirect databases from 2020 to 2023.

Results: mRNA vaccines can induce immune responses comprising both humoral and cellular immunity. Furthermore, mRNA is a fundamentally harmless vector as it is a negligible and only transient carrier of information that does not integrate into the genome. Since any protein can be expressed from mRNA without the essential to regulate the production process, mRNA construct vaccines also make extreme flexibility to development. Present investigation development on mRNA vaccines has the probable to be hasty-manufactured and to develop practical tools against infections (like SARS-CoV-2) and cancers.

Conclusion: Preclinical and clinical trials have revealed that mRNA technology offers a safe and long-lasting immune response in animal models and humans.

Keywords: mRNA Technology, Infectious Diseases, Cancer, Vaccine

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Mycobacterium tuberculosis disease and treatment review article (Review)

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Introduction: Botulinum toxin type BoNT-A (A) is a strong neurotoxin produced by Clostridium botulinum bacteria. BoNT-A is used for various therapeutic and cosmetic purposes, including the treatment of muscle disorders, chronic headaches and facial wrinkles. Headache disorders are one of the most common human disorders that most people experience many times during their lifetime. Clinical data and experience to date show that botulinum toxin type A has been used for more than a decade. It is used in the treatment of chronic migraine and results in a reduction in monthly headache attacks. Botulinum toxin acts by interacting with the SNARE complex, which inhibits the release of neurotransmitters such as glutamate, substance P, and calcitonin gene-related peptide in controlling pain is effective. In recent years, the use of botulinum toxin BTX-A has been developed to manage various headaches.

Methods: OnabotulinumtoxinA is effective not only in headache frequency and pain intensity but also in other parameters including quality of life. Tension-type headache (TTH) is the most common It is a type of chronic recurrent headache that occurs twice as often in women as in men.TTH treatment should be multi-level. It often involves taking pain medications, muscle relaxants, antidepressants, using biofeedback therapy, acupuncture, and engaging in behavioral therapy.

Results: New types of botulinum toxin selective for nociceptive neurons may be discovered or produced by recombinant DNA techniques in the next decade, and this may greatly increase its therapeutic utility.

Conclusion: This summary is related to the evolution of the use of botulinum toxin in the management of headaches in the past few decades and its role in the preventive treatment of chronic migraine and other headache disorders.

Keywords: Botulinum toxin, Clostridium botulinum, OnabotulinumtoxinA, BTX-A, Tension type headache,

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Nano-biosensors Revolutionizing Breast Cancer Detection: Current Advances and Future Prospects (Review)

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Introduction: Breast cancer is a global health concern, ranking as one of the most prevalent and deadly cancers among women worldwide. Timely and accurate detection of breast cancer is pivotal to successful treatment outcomes and patient survival. In recent years, significant strides have been made in the development and utilization of nano-biosensors as cutting-edge technology for breast cancer early diagnosis and monitoring. Nano-biosensors represent the convergence of nanotechnology and bioscience, offering unique advantages in terms of sensitivity, specificity, and real-time monitoring capabilities. These miniature sensing devices harness nanomaterial properties such as gold nanoparticles, quantum dots, graphene, and carbon nanotubes. They detect specific biomarkers associated with breast cancer at ultra-low concentrations. By interfacing with biological molecules, such as antibodies or DNA strands, nano-biosensors can selectively recognize and bind to breast cancer-related molecules, allowing for precise and rapid detection. Nano-biosensors for breast cancer detection have made remarkable progress. Researchers have demonstrated their efficacy in identifying various biomarkers, including circulating tumor cells, estrogen receptors, and HER2/neu. Moreover, these sensors offer the potential for non-invasive or minimally invasive testing, reducing patient discomfort and enhancing early diagnosis. This article delves into the current status of nano-biosensors in breast cancer detection. By shedding light on these developments, we aim to contribute to ongoing efforts to enhance breast cancer diagnosis and ultimately improve patient outcomes.

Methods: We carried out a thorough search across five different databases in order to locate papers that were published between January 2001 and August 2023 that were connected to the current status of nano-biosensors in the

detection of breast cancer. Through a series of keyword searches, a total of 450 publications were found. These searches included topics such as Nanotechnology, Nano-biosensors, Breast cancer, and Biomarkers. From among these, we chose thirty publications with full abstracts that were relevant to the topic of our research and used them in our investigation.

Results: The latest strategies, advances, and uses of nano-biosensors in breast cancer evaluation provide useful insights. It remains a critical issue to diagnose breast cancer early using point-of-care platforms, despite the wide variety of reports that have been published in this field. Initially, evaluating breast cancer is challenging because of the very low and wide variety of biomarkers. While nano-biosensors are more precise and faster than traditional methods for detecting biomarkers, physicians are concerned about the use of nano-biosensor-based point-of-care methods due to inaccurate results, like overestimation. Breast cancer early detection is challenging due to the lack of point-of-care diagnostic technology, insufficient sensitivity, selectiveness, and specialized knowledge that leads to false positives. POC diagnostic devices are needed by BC oncologists. Several studies have been carried out on developing small biosensors with less energy consumption and faster detection rates.

Conclusion: Researchers have worked on developing biosensors to identify biomarkers of breast cancer over the past few years. Nanotechnology and novel developments have made biosensors a crucial and beneficial tool for detecting BC. Identifying BC biomarkers via electrochemical biosensors has made significant advancements in recent years because of nanotechnology and biosensor methods. Even though medical diagnosis has advanced considerably in the last decade, there remain great challenges associated with traditional medical diagnosis. These challenges include a lack of POC devices, expert knowledge, low sensitivity, and selectiveness resulting in false positives. BC oncologists need POC diagnostic tools. Several studies have been conducted in order to develop small biosensors that consume less energy and have a shorter detection time.

Keywords: Nanotechnology, Nano-biosensor, Breast cancer, Biomarker, Point-of-care

Nanobiosensors food quality and safety assessment with a focus on the bacterial pathogen (Review)

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Introduction: Food poisoning is one of the defensive tools that microorganisms use when they use nutrients as a source of growth. It is due to this fact that microbes ruin food, ruin its taste, and can even cause human infection, which can be fatal in some cases. Furthermore, the food industry also has to deal with issues related to the adulteration of foods and the protection of brands. Food adulterants and contaminants at low levels are difficult to detect using routine detection systems. By utilizing nanoparticles as a detection method, a very sensitive method for finding toxic chemicals as well as microorganisms has been developed. With the use of nanosensors, disease-causing bacteria can be detected and treated. Indicators such as time temperature and oxygen content can be used to monitor the freshness of food. Using invisible nanobarcodes, brands can be protected and product authenticity assessed. The overall goal of food security is to be improved through the use of nanosensors that have unique properties. Using nanomaterials as a tool to measure food quality is the focus of this article.

Methods: A substantial amount of research has been conducted during the period between 2000 and 2020 on the assessment of the quality and safety of food, focusing in particular on the use of advanced nanobiosensors in order to detect bacterial pathogens. In order to retrieve relevant studies published during this period, several renowned databases have been used, including Scopus, PubMed, ScienceDirect, and Google Scholar, being among them. A search strategy was used in which published literature related to nanobiosensors for the detection of bacteria in food was downloaded and collected. As a result, various keywords were used during the search, such as

"bacterial pathogen detection," "nanobiosensors for food safety," "Nanotechnology in food quality assessment," "microbial contamination detection," and "foodborne illness prevention." It was found that 9750 of the 10,000 studies funded were excluded from the study based on their abstracts, leaving 250 for a thorough assessment. This research selected 50 relevant articles with comprehensive abstracts to advance knowledge in the field of nanobiosensors for detecting bacterial pathogens, particularly in food safety.

Results: Biomarkers such as genetic material or whole bacterial cells are usually used to detect pathogenic bacteria in food materials. It was less time-consuming and more sensitive to isolate deoxyribonucleic acid (DNA) and detect bacteria using nanoparticles instead of conventional methods. Using magnetic iron oxide nanoparticles, the DNA of Listeria monocytogenes was isolated. Polymerase chain reaction (PCR) was used to quantify DNA isolated from milk samples contaminated with L-monocytogenes. A wide variety of bacteria can be detected by using various nanoparticles: iron oxide, bismuth nanofilms, peptide nanotubes, gold, polypyrrole nanowires, and others such as detecting Escherichia coli and Salmonella typhimurium, Staphylococcus aureus, Vibrio parahaemolyticus and Salmonella sp., Bacillus globigii. When exposed to oxygen, packaged food items lose their freshness. The oxidation of antioxidants is facilitated by oxygen, which, in turn, promotes bacterial growth. In order to achieve this, methylene blue/titanium dioxide composite nanomaterials have been developed as colorimetric oxygen indicators.

Conclusion: A nanosensor is capable of rapidly and more effectively detecting microorganisms, toxins, and adulterants than traditional sensors. A nanoparticle can also be very useful for the detection of degradable ingredients in food products, such as vitamins and antioxidants. Additionally, nanoparticles can indicate individual packs' quality and make smart, robust packaging materials. A nanobarcode protects brands from adulteration and prevents counterfeiting. Artificial smell and taste can now be sensed by nanoparticles in electronic noses and electronic tongues in a manner similar to humans. Therefore, nanoparticles have a big impact on the food industry as a whole.

Keywords: Nanoparticle, Bacterial pathogen, DNA, Food industry, Infection

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Nanoparticle-Mediated X-PDT: An Innovative Strategy to Enhance Radiation Therapy in Cervical Cancer Treatment (Research Paper)

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Introduction: Cervical cancer is a significant global health issue, necessitating the development of innovative treatment strategies. Photodynamic therapy (PDT) is an emerging approach in cancer treatment that utilizes light and photosensitizing agents to generate reactive oxygen species (ROS) for tumor destruction. However, traditional PDT has limitations in terms of tissue penetration depth and selectivity. To overcome these challenges, the concept of X-ray induced photodynamic therapy (X-PDT) has emerged in the field of nanomedicine. This novel approach involves the use of nanoparticles as radiosensitizers that can be activated by X-rays to produce ROS and enhance the therapeutic efficacy of radiation therapy. Among these nanoparticles, Copper-Cysteamine nanoparticles (Cu-Cy NPs) have demonstrated great potential as radiosensitizers. The unique mechanism of action of Cu-Cy NPs involves their ability to be activated by various forms of stimulations, including UV, X-ray, microwave, and ultrasound. Upon activation, these nanoparticles generate ROS, such as singlet oxygen and hydroxyl radicals, which induce oxidative stress and damage cancer cells. This dual activation mechanism of Cu-Cy NPs through X-rays and other forms of radiation makes them an attractive candidate for X-PDT in cancer treatment. In this study, we aimed to investigate the effect of Cu-Cy NPs as radiosensitizers on HeLa cervical cancer cells and evaluate their potential therapeutic application in enhancing the efficacy of radiation therapy.

Methods: To assess the intrinsic toxicity of Cu-Cy nanoparticles in HeLa cancer cells, we conducted viability assessments at varying concentrations using MTT assay, both in the presence and absence of radiation exposure. Subsequently, the apoptotic rate of different groups was determined using the Annexin-V/PI staining followed by the flow cytometry analysis, while cell migration was analyzed using a wound healing assay. The collected data underwent assessment through the use of appropriate statistical tests.

Results: The results demonstrated that at a concentration of 25 mg/L, Cu-Cy NPs exhibited no significant inherent toxicity on HeLa cervical cancer cells.

However, concentrations of 50 mg/L and above showed a dose-dependent intrinsic toxicity. Notably, significant differences in cell viability were observed at concentrations of 25 mg/L and higher in the presence of radiation compared to non-irradiated groups, indicating enhanced radiosensitivity of the cancer cells. The viability in the NPs alone, radiation alone, and NPs + radiation groups were 93.85%, 90.81%, and 80.46%, respectively, indicating a significant difference between the NPs + radiation group and other groups. The apoptotic rates were 10.39% for radiation alone, 6.05% for NPs alone, and 25.41% for the combination of NPs + radiation, highlighting a significant difference in apoptotic response. Furthermore, the NPs + radiation group showed a significant difference in cell migration compared to radiation or nanoparticles alone, suggesting a potential inhibitory effect on cell migration compared to the individual treatment groups.

Conclusion: In conclusion, the findings of this study suggest that Cu-Cy NPs at low concentrations do not exhibit inherent toxicity and can enhance the radiosensitivity of HeLa cervical cancer cells. The combination of these nanoparticles with radiation yielded significantly reduced cell viability, elevated apoptotic responses, and inhibition of cell migration. These results indicate the potential of Cu-Cy NPs as effective therapeutic agents in enhancing the efficacy of radiation therapy in cervical cancer treatment.

Keywords: Cu-Cy nanoparticles, X-ray induced photodynamic therapy, Cancer, Apoptosis, Cell migration

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Nanoparticles as potent agents for the treatment of Schistosoma Infections (Review)

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Introduction: A parasitic infection caused by Schistosoma species (also called the blood flukes) leads to Schistosomiasis, a parasitic disease of humans and animals. Tropical and subtropical regions are particularly prone to the disease, particularly those with poor sanitation and no access to a safe source of drinking water. Nanoparticles have been investigated as a possible alternative to routine drugs in recent years due to their effects on parasitic infections. Nanoparticles have been studied for their anti-parasitic properties in vitro and in vivo and have shown promising results for treating parasitic diseases. This systematic review provided an overview of nanoparticle therapy for Schistosoma diseases.

Methods: Two researchers conducted a systematic search using the keywords "parasitism," "Schistosoma," "anti-Schistosoma activity," "metal nanoparticles," "nanoparticles," "polymer nanoparticles," "gold nanoparticles, "PLGA nanoparticles," and "nanoemulsions" from five English databases from 2000 to 2022, including europePMC, ScienceDirect, Ovid, Scopus, PubMed, and Cochrane. 500 studies were selected for the initial search. After removing duplicate, unrelated, and full-text articles, 19 were chosen according to the inclusion and exclusion criteria.

Results: Nanoparticles such as gold nanoparticles, liposomes, and Chitosan nanoparticles were the most common ones used to treat Schistosoma infections. In the reviewed studies, nanoparticle-loaded synthetic and herbal drugs showed an enhanced ability to combat Schistosoma larvae and adults. Nanotechnology includes nanoemulsions, liposomes, and nanoparticles for drug delivery. Schistosoma spp. has been successfully treated with these drug delivery systems in vitro and in vivo. A number of physicochemical properties must be taken into account before designing metallic nanoparticles (MeNPs) or specific nanosystems, including complexes of MeNPs with drugs attached to the shells. There are a number of factors that influence their dispersion, including surface charge, shape, surfactant type, and shell

molecules designed to ensure precise molecular interactions with parasites. Nanoparticles can be surface functionalized with aptamers, antibodies, peptides, and antibodies-like ligands to target the schistosome tegument receptor proteins and genes directly. As a result, schistosomes cannot import nutrients from the host due to the suppression of receptor genes/proteins. As a result, the parasite cannot maintain solute balance and evade the immune system. A possible way to develop anti-schistosomal drugs can be to explore and target the receptors and proteins present on the schistosome tegument.

Conclusion: By re-formulating existing drugs into site-specific targeted drug delivery systems, nanomaterials-based drug delivery systems offer effective and enhanced alternative therapies. Many NTDs can be controlled safely and with reduced adverse effects with various nanoformulations (polymeric nanoparticles, liposomes, metal nanoparticles, solid-lipid nanoparticles). The results obtained show that nanoparticle-mediated drug delivery improves efficacy through targeted delivery increased targeting efficiency, and higher bioavailability at the site of disease.

Keywords: Schistosoma, Parasite, Nanoparticles, In vitro, In vivo,

Nanoparticles as therapeutic options for treating multidrug-resistant bacteria (Review)

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Introduction: The potential for medication delivery in nanostructures is a major driver of interest in this field of medicine. It's interesting to note that the first medication delivery methods using nanoparticles appeared in the early 1990s. Since then, a number of new-generation nanoparticles with fresh medicinal approaches have been created. Therapeutic and diagnostic nanoparticles fall under two categories: inorganic (AgNps, AuNps, CuONps, ZnONps, TiO2Nps, MgONps, CaONps, Fe2O3Nps, MnO2Nps, etc.) and organic (liposomes, polymeric NPs, micelles, solid lipid Nps (SLNs), nanostructured lipid carriers (NLCs), nanocapsules, nanotubes, quantum dots, dendrimers, emulsions, nanogels, and vesicles). This study looked into the use of nanoparticles as therapeutic alternatives for multidrug-resistant bacteria.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Several inorganic nanoparticles have been successful in clinical studies and have been developed in the clinic for several applications. Organic nanoparticles have frequently been used in vaccine production and as drug delivery agents. Organic nanoparticles delivered intravenously as treatments for several diseases are also available (Petros and DeSimone 2010). Organic and inorganic nanoparticles have some distinct advantages over several intravenously administered pharmaceutical products. Compared to free drug counterparts, many organic nanoparticles can be fabricated to provide enhanced drug protection, controlled release, prolonged circulation and enhanced target to specific tissues. Moreover, the stimuli-responsive functions emanating from the surface plasmon resonance of inorganic nanoparticles give them an advantage over individual drugs or molecules. Nanomaterials have been effective against several microbes. A study by Sarwar et al. showed that ZnONps form a complex with cholera toxin, compromise its structure, and stop its interaction with receptors present in the erythrocytes. Also, M. tuberculosis showed in vitro susceptibility to AgNps, TiO2, and SeNps, although their mechanism of action remains unclear. AgNps loaded into Ti nanotubes showed promise against biofilm cells formed by MRSA. Its mechanism of action was via the release of Ag+. Also, lipid-

coated MSNps loaded with colistin and conjugated with LL-37 showed activity against P. aeruginosa-associated pulmonary infections through an isoniazid bactericidal effect. It has also been reported that bacteria exposed to AgNps upregulate genes responsible for protecting against oxidative stress (soxR, oxyR, sodB, sodA) and genes responsible for converting hydrogen peroxide to oxygen. In their investigation, Zhang et al. (2018) showed that Al2O3Nps and ZnONps accelerate mutagenesis and the emergence of multiple resistance. According to the investigation, two nanoparticles increased mutation frequency and an increase in multi-antibiotic resistance in the mutation compared to the controls. The nanoparticles also enhanced intracellular ROS, leading to a rise in the frequency of antibiotic resistance mutagenesis.

Conclusion: It is becoming clear that nanoparticles have the power to alter clinical treatment by enhancing existing medicines or introducing novel therapeutic agents. Studies on the toxicity and biocompatibility of the various combinations are required for translation into clinical practice. The processes by which bacteria resist nanoparticles have not yet been fully investigated, and they require considerable attention. Future research should make use of the adaptive mechanisms of microbial resistance to nanoparticles in order to prevent the problem of resistance associated with traditional antibiotics. Nanomaterials' distinctive qualities will enable them to revolutionize technology in the next years. Research on nanoparticles should focus on ways to lessen their hazardous effects on humans and increase their bioavailability, nevertheless. However, one important target area of nanoparticle research should be to reduce their toxic effect on humans and enhance their bioavailability and stability.

Keywords: Nanoparticles, resistant bacteria, ZnONps

Nanotheranostic platforms in cancer diagnosis: A review of recent medical imaging advancements (Review)

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Introduction: The application of nanotheranostics has gained significant attention for its broad utility in cancer therapy and molecular imaging. Nanoparticles show great promise for early cancer detection. However, it is important to thoroughly examine other factors such as drug release, bio-distribution, accumulation in target tissues, and treatment effectiveness. Recent studies on the use of nanotheranostics as a contrast agent in various imaging modalities. The main objective of this review is to explore the latest developments in nanotheranostics for cancer diagnosis.

Methods: We searched PubMed and Scopus databases and imported relevant articles into citation manager software. After screening, we reviewed 15 completely relevant papers.

Results: After a thorough review of the papers, it has been discovered that the use of nanotheranostics platforms has been combined with different imaging modalities for the early detection of cancer. These modalities include magnetic resonance imaging (MRI), computed tomography (CT), ultrasound, positron emission tomography (PET), and a combination of these in hybrid imaging. It is essential to consider that MRI has limitations, including low sensitivity and long imaging time. To enhance its signal, contrast agents can be employed, which can either be negative (ferromagnetic) or positive (paramagnetic). Gadolinium is a commonly used contrast agent in MRI, but its short lifetime during blood circulation presents a challenge. To address this, low molecular weight contrast agents can be fused to macromolecules like polysaccharides, such as pullulan. Ultrasound is a real-time non-invasive method with high soft tissue image contrast. Contrast agents used in this modality are non-microbubbles including echogenic liposomes, perfluorocarbon nanodroplets, solid nanoparticles, and gas-filled microbubbles. On the other hand, contrast media, such as iodine, tungsten, and barium, are commonly used in CT to improve soft tissue contrast. PET/C is often used in conjunction with CT for multi-modality imaging. Also, PET/MRI

imaging techniques can detect lesions and tumors from both functional and anatomical perspectives. These techniques can be effective in diagnosing prostate, breast, and lung cancer by coating SPIONs with N-trimethyl chitosan (TMC) and targeting ligands like bombesin (BN), and using the chelator S-2-(4-isothiocyanato benzyl)-1,4,7,10-tetraazacyclododecane tetraacetic acid (DOTA).

Conclusion: Nanotheranostics is of great importance in the early diagnosis of cancers especially when combined with the advantages of various imaging modalities. Nonetheless, further studies are needed to investigate the properties and pharmacokinetics of nanotheranostics in various models in vitro and in vivo for their clinical applications.

Keywords: Nanotheranostics, Cancer Diagnosis, Magnetic Resonance Imaging, Computed Tomography

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Natural carotenoid crocin induced toxic effects on gastric adenocarcinoma cells in vitro (Research Paper)

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Introduction: Crocin is one of main carotenoids found in saffron (Crocus sativus L.). This agent has a wide range of pharmacological activities such as neuroprotective, cardioprotective and antitumor properties. Many studies have shown that crocin exerts its biological effects through its strong antioxidative action. Gastric cancer is a global health problem, with more than 1 million newly diagnosed cases annually. Incidence and mortality rates of gastric cancer have declined during recent years, however, this neoplasm remains the third leading cause of cancer-related death. The present study was designed to assess the toxic effects of crocin on human gastric adenocarcinoma cells in vitro.

Methods: To assess the cytotoxicity of crocin, MKN-45 cells (a human gastric adenocarcinoma cell line) were treated with 2, 4, and 6 mM of crocin for 24, 48, and 72 hours. Cell viability was then determined by alamarBlue assay, which is based on the reduction of dark blue resazurin into pink resorufin by cellular enzymes. In addition, the viability of human normal fibroblasts (HFF-3 cell line) was also evaluated after 72 hours treatment with 2, 4, and 6 mM crocin

Results: The effects of crocin on MKN-45 cells was assessed by calculating the cell viability after treatment with different concentrations of crocin during 3 consecutive days. Our results showed that crocin induced toxicity in a dose- and time-dependent manner. After 24, 48, and 72 hours treatment with 2 mM crocin, the cell viability was calculated to be 85.9%, 78.6%, and 74.3%, respectively. Meanwhile, 54.5%, 53.9%, and 34.8% of MKN-45 cell were alive upon 24, 48, and 72 hours treatment 4 mM crocin, respectively. Moreover, 24, 48, and 72 hours treatment with 6 mM crocin reduced MKN-45 cell viability

down to 38.1%, 33.2%, and 27.1%, respectively. Worth to mention, toxicity of crocin was also observed on normal cells, as 50.9%, 27.4%, and 17.3% of HFF-3 cells were alive after 72 hours treatment with 2, 4, and 6 mM crocin, respectively.

Conclusion: To sum up, our findings indicated that crocin has toxic effects on gastric adenocarcinoma cells and normal fibroblasts in a dose- and time-dependent manner. Further research is needed to elucidate the molecular mechanism of crocin action.

Keywords: Crocin, Gastric cancer, Cytotoxicity, Natural carotenoid, in vitro assay.

Natural immunosuppressants as a treatment for chronic insomnia targeting the inflammatory response induced by NLRP3/caspase-1/IL-1β axis activation: a scooping review (Review)

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Introduction: Chronic insomnia is an inflammatory-related disease with an important pathological basis for various diseases which is a serious threat to a person's physical and mental health. So far, many hypotheses have been proposed to explain the pathogenesis of insomnia, among which inflammatory mechanisms have become the focus of scientific attention. In this regard, the aim of the present scooping review is to evaluate the potential benefits of natural compounds in treatment of chronic insomnia targeting nucleotide-binding oligomerization domain (NOD)-like receptor-pyrin-containing protein 3 (NLRP3)/caspase-1/IL-1β axis as one of the most important activators of inflammatory cascades.

Methods: Relevant articles were identified through searches of MEDLINE, PubMed, International Pharmaceutical Abstracts, EMBASE Drugs and Pharmacology, and Current Contents/Clinical Medicine.

Results: The data show that compounds that have the potential to cause inflammation induce sleep disorders, and that inflammatory mediators are key molecules in regulating the sleep-related activity of neurons. In the inflammatory process of insomnia, the role of NLRP3 in the pathogenesis of insomnia has been gradually considered by researchers. NLRP3 is an intracellular sensor that recognizes the widest range of pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns

(DAMPs). After identification and binding to damage factors, NLRP3 inflammasome is assembled to activate the caspase-1 and IL-1β. Increased production and secretion of IL-1β may be involved in central nervous system dysregulation of physiological sleep

Conclusion: The current scooping review reports the potential benefits of natural compounds that target NLRP3 inflammasome pathway activity and highlights the hypothesis which NLRP3 /caspase-1/IL-1β may serve as a potential therapeutic target for managing inflammation and improving symptoms in chronic insomnia.

Keywords: Chronic insomnia, IL-1β, NLRP3, Plant-derived immunosuppressants

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Natural remedies can help treat vaginitis (Review)

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2.

Introduction: Vulvovaginit is one of the most widespread gynecological disorders among adolescent and childhood female.The vaginal environment is home to numerous microorganisms who have mutualistic relationships with each other and their hosts. Lactobacillus species as an indicator species among the natural microorganisms in the vaginal environment is responsible for the production of antimicrobial compounds such as hydrogen peroxide, lactic acid and bacteriocin-like substances. Vaginitis occurs when the micro-organisms unbalanced in the vaginal environment finally vaginal environment are favorable to the growth of anaerobic bacteria and producing lactic acid and hydrogen peroxide by the Lactobacillus species. Lactic acid produced by lactobacillus causes acidification of the vaginal environment with PH (3.5-4.5) which promotes Lactobacillus ssp. The polymicrobial biofilm in the vaginal epithelium could be created by the microorganism in vaginosis. The usual type of vulvovaginit are bacterial vaginosis (BV), candida vaginitis (CV), Trichomonas vaginalis (TV).Volvovaginit treatment is normally prescribed using antibiotics such as metronidazole, clindamaysin for BV and azole group for CV Although the treatment shows to be effectively remedied and alleviate signs and symptoms of infection in the long term but there is a possibility of relapse of infection very common. Therefore, the use of alternate therapies is suggested, which includes 1. Home remedies 2.Phytotherapy 3.Lactobacillus therapy 4. Vaginal douche 5. Yogurt therapy 6.Treatment with honey, royal jelly and propolis are bee products that have antimicrobial properties due to their flavonoid and phenolic compounds. They are used in the treatment of vaginitis. Other new strategies to increase the rate of treatment for vaginitis include the use of prebiotics, probiotic, acidifying agents, antiseptics, vaginal microbiota transplantation, and phage endolysins.

Methods: Use of the antibiotics causes to distribute normal flora vagina and reduce lactobacillus and other microorganism of the normal flora vagina and could more grow fungi and bacteria finally increase resistance to antibiotics. Past research show use natural materials for treatment vaginit in addition to the inhibitory properties of microorganisms, it improves the symptoms of disease and prevent the recurrence of the symptoms of disease.

Results: The treatment of infection vaginitis whit antibiotics has acceptable results however whit high recurrence rate after treatment.. Natrule trapy vaginitis is the reduction of side and systemic effect and decline the risk of bacterial resistance.

Conclusion: The high recurrence of infection vaginitis is attributed to several reasons, including an increase in bacterial resistance to certain antibiotics 2. The presence of biofilm infection decreasing the effect of antibiotics and produces non-sensitive species 3.The presence of a biofilm in the infection makes hard to wipe out the infection 3.More than one species led to reduction anti-microbial properties to kill bacteria and wipe out biofilm. Formulation of antibiotic recommend for vaginitis are not efficient because of their leaking, lack of proper drug release or short stay in the vagina. Treatment of vaginit by natural compounds are effective whit out harmful effect and whit out disrupt in the natural flora of vaginal.

Keywords: 1.Vulvovaginit 2.Bacterial resistance 3.Alternate therapes 4.Phenoli compounds 5.Flavonoid compounds

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Neisseria gonorrhoeae review article (Review)

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1.
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Introduction: Neisseria gonorrhoeae (GC) is a human specific pathogen that cause the sexually transmitted infection and in (N. gonorrhoeae , gonorrhea) is a gram negative bacterium with a wide range of clinical presentation. N.gonorrhoeae is an obligate human pathogen that colonizes mucosal surfaces of the urogenital tract , pharynx , rectum , and conjunctiva , where it stimulates robust neuthrophil recruitment. Sexually transmitted infections (STIs) are a major global public health problem and among the most common infectious diseases. Gonorrhoea is an STI that affects only humans, caused by the bacterium Neisseria gonorrhoeae. Gonococcal infection in humans does not generate an effective immune response in most cases, which contributes to both transmission of the pathogen and reinfection after treatment. Neisseria gonorrhoeae is known to evade and suppress human immune responses through a variety of mechanisms. Gonorrhea is considered an urgent threat to public health with an estimated 87 million cases occurring annually worldwide, growing antimicrobial resistance, and the absence of a gonococcal vaccine.

Methods: N.gonorrhoeae infection starts with the adhesion of gonococci to epithelial cells, followed by local cellular invasion. Gonorrhea has multiple surface proteins that facilitate adhesion. N. gonorrhoeae utilize pili to initiate adhesion to epithelial cells. Hair-like appendages, pili, cover the bacterial surface. Their ability to lengthen and retract allows the bacteria to attach from a distance and move closer to the epithelial cells, promoting cellular invasion. its ability to develop resistance to antimicrobials and in the antigenic variability by which it evades host defences, thus persisting and often causing asymptomatic (and undetected) infection. infection in men and the endocervix infection in women are the common causes of gonorrhoeae. This damage the columnar epithelium of the endocervix and cause pain during sexual contact, an aching feeling while urinating and abdominal vaginal emission.

Results: The continued worldwide incidence of gonorroeal infection , coupled with the rising resistance to antimicrobials and the difficulties in controlling the diseas in developing countries , highlights the need to better understand the molecular basis of N. gonorrhoeae infection .

Conclusion: In females, N. gonorrhoeae most commonly infects the cervix, resulting in cervicitis. When female patients with gonococcal urogenital infections have symptoms, they may complain of vaginal discharge, dysuria, or pelvic pain. Az no gonococcal vaccine is available , prevention relies on promoting safe sexual behaviours and reducingSTI associated stigma , which hinders timely diagnosis and treatment therapy increasing transmission.

Keywords: Neisseria gonorrhoeae- infection- pathogen- sexually

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Neurocognitive Impact of ADHD in Children with Learning Disability and Psychiatric Disorders (Review)

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Introduction: Cognitive disorders are divided into three common neurological disorders: attention deficit/hyperactivity disorder (ADHD), developmental dyslexia and developmental dyslexia. An overview of the research situation shows that most studies use repetitive transcranial magnetic stimulation (rTMS) techniques and transcranial direct current stimulation (tDCS) and unequal distribution among clinical conditions. The risk of major depressive disorder (MDD) increases significantly in young adults with attention deficit/hyperactivity disorder (ADHD), but the underlying mechanisms are not well understood. This review explores ADHD-specific neurocognitive disorders as possible underlying mechanisms for ADHD-depressive comorbidity. Attention deficit/hyperactivity disorder (ADHD) in adulthood and dementia with Lewy bodies (DLB) have many cognitive and non-cognitive similarities. Overlapping features between both disorders complicate differential diagnosis. We also investigated the prevalence and correlation of neurocognitive and psychiatric disorders among students in Uganda.
Methods: In this cross-sectional study۳۲۲ ، students aged 5-17 years participated in Waqisu ،Uganda. We evaluated battery and psychiatric disorders (major depressive disorder (MDD), attention deficit hyperactivity disorder (ADHD), generalized anxiety disorder (GAD), and substance use disorder (SUD)) using the parent version of the Child and Adolescent Symptoms Questionnaire 5 and the Self-Report 4R Youth Questionnaire. The aim of this study was to determine the neurocognitive impact of ADHD in children with learning disability and psychiatric disorders

Methods: This was a narrative review study conducted in 2023 by searching keywords such as neurocognitive, ADHD, psychiatric disorders, and non-invasive brain stimulation in reliable databases such as: Scopus, Elsevier,

Web of Science, and PubMed. Finally, 15 articles were found and 10 articles were included in the study.

Results: According to the literature studies, non-invasive brain stimulation (NIBS) has been highlighted as a powerful tool for promoting neuroplasticity and an attractive approach to support cognitive modification. Here we have a systematic review of 26 articles using NIBS to improve given the usefulness of NIBS, the results are promising but ambiguous. Twenty-three papers reported beneficial effects, but many of these effects were repeated only once or only to some extent, and some studies even reported harmful effects. In addition ‹ most studies differed in at least one main aspect ‹NIBS was applied ‹ questionnaires and cognitive tests performed or age group surveyed ‹and the sample size was mostly small. During acute depression, children and adults showed cognitive deficits that overlapped with some ADHD-related disorders. The findings of hospitalized patients ‹high-risk individuals and several prospective studies indicate that subsets of these common disorders ‹ especially executive dysfunctions (selective attention ‹verbal fluency ‹working memory) and long-term memory problems ‹are markers of depression risk. We discuss whether and how these specific neurocognitive mechanisms may mediate growth pathways from ADHD to depression. If replicated by longitudinal studies ‹these findings may guide future prevention strategies.There was also a combination of findings from the individual study showing that there were deficits in working memory for late life ADHD and deficits in the areas of attention ‹memory ‹language and visual abilities for DLB. The results were limited by small samples and a lack of data in some cognitive domains.

Conclusion: Further studies are needed to investigate the potential of NIBS in modifying cognitive functions. Finally ‹we discuss potential warnings and future directions. We argue that if we address these challenges adequately, NIBS could be feasible, with potential benefits in the treatment of neurological disorders that could prove very beneficial.

Keywords: Neurocognitive, ADHD, Psychiatric Disorders and Non-invasive Brain Stimulation

New methods to prevent the transmission of genetic syndromes in fetuses (Review)

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Introduction: Genetic disorders stem from mutations, in DNA, which may either be inherited from parents or occur spontaneously. These disorders can lead to cognitive disabilities greatly impacting the lives of individuals and their families. Additionally these syndromes can be passed down to fetuses during pregnancy resulting in challenges and health issues. Recent years have witnessed advancements in the identification and prevention of syndromes in fetuses. This essay aims to explore novel approaches to hinder the transmission of syndromes. Pre Implantation Genetic Diagnosis (PGD) emerges as a technique for examining embryos genetic makeup before implantation. By employing this method the transmission of syndromes to fetuses can potentially be avoided. During PGD a few cells are extracted from the embryo for DNA analysis to detect any genetic mutations present. Embryos devoid of mutations are then chosen for implantation. PGD is applicable not for gene disorders but also for chromosomal abnormalities and various other genetic conditions. The success of PGD is evident through its ability to prevent the transmission of syndromes. For instance it has been effectively employed in averting the passing, on of fibrosis—a disorder that primarily affects the respiratory system and digestive tract. PGD has also been employed to hinder the transmission of Huntingtons disease, which's a condition that leads to difficulties, with movement and cognitive deterioration. PGD has some limitations. The success rate of PGD depends on the quality of the embryos and the accuracy of the genetic testing. PGD can also be expensive and time-consuming. Additionally, PGD may not be suitable for all couples, as some genetic mutations cannot be detected using this technique.

Methods: Non-Invasive Prenatal Testing (NIPT) Non-invasive prenatal testing (NIPT) is a technique used to detect genetic abnormalities in fetuses during pregnancy. NIPT is a blood test that analyzes the DNA of the fetus that is present in the mother's blood. NIPT can detect chromosomal abnormalities, such as Down syndrome, and can also detect some single gene disorders. NIPT is more accurate than traditional prenatal screening tests, such as the triple screen or quad screen. NIPT can help parents make informed decisions about their pregnancy and can help healthcare providers prepare for the care of the newborn. NIPT has some limitations. NIPT cannot detect all genetic

abnormalities, and false positive and false negative results can occur. Additionally, NIPT is not a diagnostic test, and further testing may be required to confirm the results. Gene Editing Gene editing is a technique used to modify the DNA of cells, including human cells. Gene editing can be used to correct genetic mutations that cause genetic syndromes. Gene editing involves cutting and replacing DNA segments using specialized enzymes. Gene editing can be performed on embryos before implantation, which can prevent the transmission of genetic syndromes to fetuses. Gene editing has been successful in correcting genetic mutations in animal models and in human cells in the laboratory.

Results: Gene Therapy Gene therapy is a technique used to treat genetic disorders by replacing or repairing the mutated genes. Gene therapy can be used to treat genetic syndromes in fetuses. Gene therapy involves delivering healthy genes to the cells of the body using viruses or other delivery methods. Gene therapy has been successful in treating some genetic syndromes. For example, gene therapy has been used to treat severe combined immunodeficiency (SCID). Gene therapy has some limitations. Gene therapy can be expensive, and the long-term effects of gene therapy are not yet known.

Conclusion: Genetic syndromes can cause lifelong disabilities and medical challenges for individuals and their families. In recent years, significant advances have been made in identifying and preventing genetic syndromes in fetuses. Pre-implantation genetic diagnosis (PGD) is a technique used to test embryos for genetic mutations before implantation. Non-invasive prenatal testing (NIPT) is a technique used to detect genetic abnormalities in fetuses during pregnancy. Gene editing is a controversial technique that can be used to modify the DNA of embryos, and gene therapy is a technique used to treat genetic disorders. These new methods can help prevent the transmission of genetic syndromes in fetuses and improve the quality of life for individuals and their families. However, these techniques also raise ethical concerns and have limitations that need to be carefully considered.

Keywords: fetuses-NIPT-Gene Editing-Gene Therapy

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Nocardia disease, treatment review article (Review)

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Introduction: Nocardiosis is a gram _positive, ubiquitous, soilborne belongs to the Family of aerobic actinomy cetes that seem like branching, .filamentous rods on microscop This genus Nocardia includes more then eighty species, thirty of which could affect .humans There is also a species of Nocardia a called Nocardia farcinica, which is very similar to.

Methods: An interesting case from North india was investigateg by scientisis, which is septic embolism and infectious endocarditis caused by Nocardia farcinica. A very rare phenomenon.

Results: Paucivorans by metagenation sequencing (mNGS) of BALF. The patient was treated with trimethoprim_sulfamethoxazole

Conclusion: Paucivorans by metagenation sequencing (mNGS) of BALF. The patient was treated with trimethoprim_sulfamethoxazole

Keywords: Nocardia Bacteria Gram positive

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Nosocomial infections resistant to Pseudomonas review article (Review)

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Introduction: Nosocomial infections are also known as hospital-acquired associated infections.The agents that are usually involved in hospital-acquired infections include Streptococcus spp., Acinetobacter spp., enterococci, Pseudomonas aeruginosa, coagulase-negative staphylococci, Staphylococcus aureus, Bacillus cereus, Legionella and Enterobacteriaceae family members, namely, Proteus mirablis, Klebsiella pneumonia, Escherichia coli, Serratia marcescens.

Methods: Material methods: Nosocomial pathogens can be transmitted through person to person, environment or contaminated water and food, infected individuals, contaminated healthcare personnel's skin or contact via shared items and surfaces. Mainly, multi-drug-resistant nosocomial organisms include methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, Pseudomonas aeruginosa and Klebsiella pneumonia, whereas Clostridium difficile shows natural resistance.Excessive and improper use of broad-spectrum antibiotics, especially in healthcare settings, is elevating nosocomial infections.

Results: Results:This study was planned to delineate prevalence of MDR P. aeruginosa in nosocomial infection patients, and to screen for ESβLs producing P. aeruginosa with typing of P. aeruginosa isolates in Menofia University Hospitals (MUH), Egypt. Our study included 287 inpatients admitted to Menoufia University Hospital and having different nosocomial infections. Samples from medical staff and from hospital environment were collected. Antibiotyping of P. aeruginosa isolates were determined. MDR and ESBLs P. aeruginosa were detected. Plasmid DNA analysis and pyocin typing were done.

Conclusion: Conclusion: This study investigated the correlation between fluoroquinolone (ciprofloxacin or levofloxacin) use and rates of fluoroquinolone resistance in Pseudomonas aeruginosa isolates from patients with nosocomial infection at a medical centre in Taiwan.

Keywords: infection, Pseudomonas, resistant, isolate, medical

Novel wound dressing based on probiotic/chitosan (Research Paper)

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Introduction: Dermal wound healingis a complex biological process, which includes four overlappingsteps. These are the in?ammatory phase immediately after thelesion has occurred, the migratory, proliferative and maturationphase resulting in remodeling

Methods: The chitosan solution (10%) was added to supernatant Bifidobacterium . For wound treatment investigation, 45 male wistar rats divided in 3 groups; control negative (without treatment), chitosan film group, and chitosan/supernatant film group. A full thickness wound was created on the back of the animals and treated with corresponding wound dressing. After direct measurement of wound diameter, 3 rats were sacrificed from each group on day 3, 7, 14 and 21. The wound healing process was identified by histological analysis

Results: Our results showed in treatment accelerates the wound healing process by reduce the inflammatory phase , and the proliferative phase starts sooner in the wound healing process.

Conclusion: chitosan/probziotic can be used as wound dressings to promote wound healing.

Keywords: Wound-healing , Chitosan, Probiotic

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Omicron variant (B.1.1.529): Emergence, characteristics and prevention (Review)

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Introduction: Coronavirus disease 2019 (COVID19) has created a significant threat to global health and has attracted attention from all over the world since its outbreak. Recently, a new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported to World Health Organization (WHO) from South Africa on November 24, 2021, recorded as Omicron variant (B.1.1.529), as a variant of concern (VOC). This variant harbors a large number of mutations particularly, in the receptor-binding domain (RBD) of spike which is different from the previous VOC Alpha, Beta, and Gamma variants. Therefore, it has raised global concerns about transmissibility, disease severity and immune evasion.

Methods: In this review, articles were searched from 2020 to 2023 in the Google Scholar, Science Direct, PubMed and Scopus databases. In addition, Farsi and English keywords related to the aim of the study were used to search for articles. Finally, 30 articles were considered for the review.

Results: This review has focused on the emergence and characteristics of the Omicron variant, and possible strategies to prevent and overcome the prevalence of the Omicron variant.

Conclusion: There are many questions concerning Omicron strain, which is the most mutated strain that has emerged. Although it is possible that other strains may evolve after Omicron and make the epidemic control more complicated, fortunately, according to the past experiences, we can prevent the spread of other variants.

Keywords: COVID-19, Omicron, SARS-CoV-2

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Organoid of ovarian cancer: genomic analysis and drug screening (Research Paper)

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Introduction: Cancer is one of the leading causes of deaths worldwide . Ovarian cancer (OC) has the highest mortality rate among gynecological tumors that threaten women's health and life . Most cases (70%) are diagnosed at an advanced stage because the clinical manifestations of early OC are hidden or unspecific. Traditional and novel treatment schemes for this illness have progressed in the past decades, but the lack of early diagnosis and the poor efficiency of postoperative chemotherapy restrict the improvement in the 5-year survival rate of patients with OC . Therefore, research on OC focuses on determining highly specific and sensitive tumor markers for early diagnosis and prognosis evaluation (diagnostic aspect) and on exploring new strategies (therapeutic aspect), such as targeted therapy and immunotherapy. Preclinical models that can accurately recapitulate the biological characteristics of tumors in vivo are essential in this process. OC cell lines used to have a dominant role in OC biology, but have been gradually replaced by patient-derived xenograft (PDX). In the era of precision medicine, preclinical research platform derived from each individual has become indispensable, and high-throughput genomic analysis has been widely used to search for effective personalized treatment methods. Organoid is a powerful tool for precision medicine and drug screening . This technique can maintain the characteristics of tumor and its microenvironment in vivo to the greatest extent and can rectify the shortcomings of single cell lines in testing new drugs. The organoid maintains homology with primary tumors for a long time; hence, its drug sensitivity is better than that of cell lines during drug screening. Tumor-like organs are easy to replicate and pass on to form a biobank, which can be used for large-throughput gene analysis and drug screening. These organs can maintain the genetic heterogeneity of tumors and can mimic a hypoxic microenvironment. The organoid is a 3D tissue model directly induced by stem cells and a newly emerged preclinical model. Its application has been extended to many fields. At present, the organoid can be produced from primary prostate, colon, and pancreatic cancers . The OC organoid can multiply normal and precancerous cells, and its success rate is higher than those of PDX and spheroid. Organoids can be cultured from

different tissues of different patients, such as primary and metastatic tumors, blood tissue, ascites, pleural effusion drainage, and normal FT and OSE.

Methods: This systematic study was mentioned using key words and referring to reliable scientific databases such as Scopus, PubMed, Google Scholar and ProQuest from the studies that were conducted until 2023 and a total of 15 articles were reviewed.

Results: The ovarian cancer organoid is a stable tumor model that can be used for gene analysis, predicting drug sensitivity, and searching for specific biomarkers. This cell culture model can be used for gene manipulation and drug screening. Organoid is a useful tool in the study of targeted gene therapy and provides a suitable environment for studying immunotherapy. The organoid can establish various OC subtypes, including precancerous cells and normal tissues and therefore can be used to study tumor evolution. Salama's team used organoids to show the process of Helicobacter pylori colonization in gastric epithelium that may cause cell transformation . Scanu's team used gallbladder organoids to assess the role of Salmonella in the development of gallbladder cancer and showed that this infection can activate Akt and MAPK signaling pathways. In the future, the organoid must be employed to study the evolution from normal tissues, precancerous lesions, low-grade malignancy, and finally to high-grade malignancy.The main gene changes are analyzed to achieve early detection, prevention, and treatment. The results will be of great importance for the early screening of OC.

Conclusion: As a new preclinical model, the organoid needs improvements, specifically its success rate. Its tumor microenvironment is single and lacks matrix, blood vessels, and immune cells. Further modifications can render the Ovarian Cancer organoid an efficient and robust method for the primary organ culture of gynecological tumors and a highly reliable research approach for targeted therapy and immunotherapy.

Keywords: Drug screening; Immunotherapy; Organoid; Ovarian cancer; Targeted therapy.

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Overview of the application of Exosomes as promising alternatives: A new approach in Regenerative Medicine (Review)

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Introduction: Exosomes are extracellular nanovesicles that are secreted from various ranges of cells including different stem cells representing features and contents of the source. The unique characteristics and efficient functions of exosomes have made them more preferable options for regenerative purposes and also drug delivery systems. Exosomes are already employed in various fields like wound healing, anti-cancer therapy, anti-aging studies, neurodegenerative diseases, as well as in cardiovascular, hepatic, pulmonary and renal tissue repair.

Methods: Literature review of current study was based on the systematic search in valid databases like PubMed, Scopus and Google Scholar. all articles containing keywords “Exosome”, “Regenerative Medicine”, “Stem cell”, and “Cell-free” in the title, published during past five years (2018-2023), have been included; then abstracts and main texts were scanned.

Results: The superiority of the exosomes is still controversial hence stem cells are more extensive and complicated for reaching full potential regeneration. evidently there are some drawbacks about exosomes like low yield and difficult manufacturing, but higher safety against neoplastic proliferation, lower antigenicity, stability and better storage, small size (entering blood brain barrier), ease of application through various routes, tissue specificity and controlled targeted therapy, better intercellular communication and signaling for improved regulation and modulation of immune and inflammatory procedures, and evidence of better results in resolving certain health problems.

Conclusion: Exosomes can be applied in regenerative medicine due to their unique characteristics and advantages over stem cell therapy, compensating the limitations and improving the functional efficiency.

Keywords: Exosomes, Extracellular Vesicles, Stem Cells, Regenerative Medicine

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OXIDATIVE STRESS AS INFERTILITY INDEX IN SEMINAL PLASMA OF OLIGOZOOSPERMIA PATIENTS (Review)

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Introduction: The male germline is particularly vulnerable to oxidative stress and DNA damage, affecting male fertility and normal embryonic development. There are many factors that influence normal semen parameters (sperm concentration, motility, morphology, count, etc.) and their abnormalities cause oligozoospermia. Oligozoospermia is defined as less than 15 106 sperm/mL of semen ejaculated. Oligozoospermia and reactive oxygen species (ROS) are associated with male infertility.

Methods: Oligozoospermia may be due to testicular factors (chromosomal disorders, obstruction, testicular trauma, varicocele, etc.) or general health condition (obesity, smoking, drug and/or alcohol use, high fever, etc.). Oxidative stress has been implicated in diseases such as cancer, diabetes, cardiovascular disease, brain disorders such as Alzheimers disease, and even female and male infertility. Spermatozoa susceptibility to oxidative damage and rapid loss of motility of spermatozoa -incubated in oxygen-rich environment confirmed that.

Results: Loss of motility due to overproduction of oxidants, increased catalase and sperm oxygen metabolism. Increased ROS activity in mitochondrial membranes and sperm plasma show protein damage, and lipid peroxidation including, hydroxyl radicals (OH), superoxide anion (O2), and hydrogen peroxide (H2O2). ROS cause male infertility, DNA damage of sperm, birth defects, pregnancy loss, impaired embryonic development, offspring defects like childhood cancer and autism.

Conclusion: Sperm plasma membranes are rich in polyunsaturated fatty acids, such as docosahexaenoic acid, which six double bonds per molecule creates an electron sink and are susceptible to oxidation and chemical and structural modifications. ROS modification causes loss of motility and impairment of membrane fusion events such as the acrosomal reaction and sperm–oocyte fusion. In addition, the level of DNA damage in mitochondrial and nuclear genomes of human spermatozoa have been identified by techniques such as sperm chromatin structure assay (SCSA), terminal deoxynucleotidyl transferase-mediated dUTP nick-end labelling (TUNEL), measurement of the DNA oxidation adduct, and 8-hydroxydeoxyguanosine (8-OHdG). Oxidative damage degree (endogenous or exogenous source) and ROS production associated with spermatogenesis disorders, male infertility, and azoospermia.

Keywords: reactive oxygen species, oligozoospermia, infertility, spermatozoa

Parasite and brain disorder: effects of Toxoplasma on Schizophrenia (Review)

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Introduction: Many scientific evidence points show the central role of the immune system in the etiopathogenesis of Schizophrenia and some related psychiatric disorders. Some factors among genetics, neuropathological, neuroimaging, and metabolic involve the immune system. Many studies indicate some degree of immune dysregulation and inflammation in the brain of individuals with Schizophrenia. Some organisms can stay in the non-replicating phase or very slow replication, called the latent phase, and cause inflammation in the brain or other organs. Finally, genetic factors are strongly associated with Schizophrenia. Thus, infection organisms that interact with host genetic factors are likely to play a central role in Schizophrenia. Although many pathogenic agents meet these criteria, the one that has been studied the most is the apicomplexan protozoan Toxoplasma gondii. Toxoplasma is classified as a pervasive pathogen and infects nearly a billion people in the world. Initial infection with Toxoplasma is associated with a few symptoms that may not be identified. It also induces lifelong cyst formation mostly in the brain and other organs like the retina and muscles. This research aims to gain a correct understanding of the relationship between Toxoplasma and Schizophrenia. By using it we can treat or induce the symptoms of Schizophrenia with the medicine that is used to cure Toxoplasma.

Methods: The present review was conducted through the electrical scientific databases including Google Scholar, and PubMed by searching with keywords including Toxoplasma, and Schizophrenia. After these articles were reviewed, a general conclusion was extracted from all the articles.

Results: The results show that children of mothers with a virulent strain of Toxoplasma infection were at higher risk of developing psychiatric disorders compared to uninfected control mothers. As noted before, most of the Toxoplasma cysts are located in the brain, so these are not accessible. To overcome this limitation there is a non-invasive, highly sensitive, and specific

method for the measurement of cysts and recognition of the latent phase, and it's called MAG1. There is a relationship between behavior changes with the number of cysts and the MAG1-positive patients, As the number of cysts and MAG1 increases, behavioral changes are more obvious. Behavioral changes include predator odor aversion and anxiety-related behavior. In one of the experiments conducted on mice, it was found that mice with a high level of MAG1(MAG1>0.5) exhibited reduced locomotor and exploratory activity, impaired object recognition memory, and lack of response to amphetamine-induced activity. These changes were not found in mice with lower levels of cyst burden(MAG1<0.5). Some changes include altered fiber density, loss of fiber continuity, reduction of synaptic protein PSD95, and synaptophysin. Gray matter volume also decreases in Toxoplasma-positive patients.

Conclusion: Many studies linked Toxoplasma to psychiatric disorders including schizophrenia. The multifaceted effects of Toxoplasma infection on neuroinflammation, neurodegeneration, and behavior are only beginning to be understood. Toxoplasma as a neurotropic pathogen may affect information processing in a wide variety of functional brain systems. Although much data points to the role of Toxoplasma infections in the pathogenesis of schizophrenia, the final documentation of this connection shows that anti-Toxoplasma drugs moderate the clinical symptoms or course of psychiatric disorders. Toxoplasma infection can open a door to understanding the complexity of human neurological disease.

Keywords: Toxoplasma, Schizophrenia

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Peptide-based antimicrobial agent against dihydrofolate reductase of Staphylococcus aureus (Research Paper)

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Introduction: Staphylococcus aureus (Sa) is one of the Gram-positive pathogens that causes a wide range of clinical diseases. This pathogen can cause many different types of infections, including skin infections, bone infections, pneumonia, and endocarditis. Conversion of dihydrofolate (DHF) to tetrahydrofolate (THF) is catalyzed by dihydrofolate reductase (DHFR) in the presence of coenzyme NADPH. THF is essential in the synthesis of adenine and guanine for DNA replication. Inhibitors of dihydrofolate reductasein S. aureus leading to pathogen death. In this research, we study peptide-based antimicrobial agent against DHFR of S. aureus by in silico approach.

Methods: The 3D crystal structures of dihydrofolate reductase (PDB ID: 3FYV) in complex with NADPH were downloaded from the Protein Data Bank. For docking operation, by using Accelrys software, co-crystallized ligand XCF300 and all water molecules were deleted from the enzyme structure. The 3D of the peptide was designed and optimized by HyperChem Professional, and then the physical and chemical parameters of the optimized peptide were obtained by the ProtParam tool. The affinity of this peptide to dihydrofolate reductase of Staphylococcus aureus was estimated by docking operation.

Results: Based on the physical and chemical parameters, the designed peptide with molecular weight: 1795.36, theoretical pI: 12.02, aliphatic index: 55.71, and grand average of hydropathicity: -2.079 is a stable peptide. Our docking results showed, designed peptide with Docking Score of -194.90 binds to the binding site of 3FYV by amino acids LYS4,HIS10, HIS7 and ARG11.

Conclusion: Designed peptide with sequence LLKKHPHHPHRRKX while having proper stability, is able to occupy the binding site of the dihydrofolate reductase of Staphylococcus aureus, to confirm the results, experimental studies on this peptide-based antimicrobial agent are necessary.

Keywords: Antimicrobial Agent, Dihydrofolate reductase, Staphylococcus aureus, In silico

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Perceived social support and related factors in middle-aged women in Shiraz (Research Paper)

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Introduction: Social support is a source of psycho-social support that is obtained from social relationships with different social networks of family, friends and others. Social support is related to important mental and psychological indicators such as quality of life, depression and satisfaction with people's lives; But the factors related to it in middle-aged women have received less attention. Therefore, the present study investigated demographic factors related to perceived social support in middle-aged women in Shiraz.

Methods: In this cross-sectional study, 256 middle-aged women of Shiraz city, who were selected by a multi-stage method, participated. The criteria for entering the study was to be between the ages of 45 and 65 and willing to participate in the study. To measure social support, the multidimensional scale of perceived social support was used. Its reliability was found to be 0.88 in the present study. SPSS22 software, T-tests, ANOVA and linear regression analysis were used to analyze the data.

Results: The average age of the participants was 51.34 ± 2.1, 89% were married and 45.1% had a diploma or higher. The average score of perceived social support was 21.23±2.71. Among the studied demographic factors, only income adequacy had a significant relationship with it ($P<0.001$) so that in people with higher income adequacy, perceived social support was also higher. Linear regression analysis showed that income adequacy predicts 15.3% of social support in middle-aged women studied.

Conclusion: Women with low income receive less social support, which needs to be paid attention to by social policymakers.

Keywords: Middle age, women, perceived social support, income adequacy

Personalized Vaccines using Nanoparticle Carriers: Revolutionizing the Fight against Helicobacter pylori-induced Gastric Infections (Review)

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Introduction: Helicobacter pylori (H. pylori) is a bacterium that annually affects a significant portion of the global population, leading to various gastric diseases. However, the emergence of antibiotic resistance has posed challenges in effectively treating these infections. In response, researchers have turned to specialized methods of medical biotechnology to propose alternative solutions. One promising strategy involves the development of personalized vaccines that take into account individual characteristics, with nanoparticles serving as carriers to enhance the immune response. The aim of this review study is to comprehensively explore the development of personalized vaccines against H. pylori-induced gastric infections, specifically focusing on the utilization of nanoparticles as vaccine carriers.

Methods: To conduct this review, relevant information from reliable sources and scientific articles in the fields of medicine, biotechnology, nanotechnology, and biological sciences was extracted. A comprehensive search was performed using databases such as PubMed, Web of Science, and Scopus. The inclusion criteria focused on articles published within the last 10 years and written in English. The search strategy specifically targeted studies related to the development of personalized vaccines against H. pylori-induced gastric infections, with an emphasis on the utilization of nanoparticles as vaccine carriers.

Results: Studies indicate that medical biotechnology, through introducing innovative techniques, has brought about the most revolutionary advancements in the field of producing effective vaccines against H. pylori. Designing and developing personalized vaccines based on genetic sequences, physiological characteristics, and individuals' medical histories,

using advanced molecular techniques, has enabled us to precisely identify specific antigens of this bacterium. In this regard, antigens possessing suitable biochemical and biological properties are selected and presented as vaccines in combination with effective carriers. In this domain, nanoparticles, due to their specific physicochemical and surface properties, are capable of influencing cells and bacteria, serving as carriers for antigens and vaccine adjuvants. These compounds are transferred to immune cells to enhance the effectiveness and stimulation of the vaccine's immune response in the individual, thus aiding in reducing vaccine-related side effects.

Conclusion: Personalized vaccines against H. pylori utilizing nanoparticles as carriers offer a promising strategy for combating this bacterium. Medical biotechnology and advanced molecular techniques have facilitated the identification of specific antigens for personalized vaccine design. Nanoparticles possess specific properties that make them ideal carriers, enhancing immune response and reducing potential side effects. This approach presents a novel solution, particularly in the context of increasing antibiotic resistance. Further research is necessary to optimize the efficacy and safety of these personalized vaccines.

Keywords: Medical Biotechnology, Personalized Vaccines, Helicobacter Pylori, Nanoparticles, Gastric Infection

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Phenotypic and genotypic characterization of carbapenemase and ESBL-producing Klebsiella pneumoniae clinical isolates (Research Paper)

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Introduction: Carbapenem-resistant clinical isolates are extending rapidly, and in recent years, carbapenem resistance has become an important health problem worldwide. This study aimed to investigate the carbapenem-resistance genes in extended-spectrum β-lactamase (ESBL) producing K. pneumoniae isolates.

Methods: Seventy-five non-duplicate clinical K. pneumoniae strains were isolated from urine, blood, sputum, and wound samples. Antimicrobial susceptibility tests for 12 different antibiotics were performed using the disk diffusion method, followed by the determination of minimum inhibitory concentrations (MIC) of imipenem and meropenem. Phenotypic detection of ESBL and carbapenemase enzymes was performed by double-disc synergy test (DDST) and modified Hodge test (MHT), respectively. Resistant isolates were further investigated for ESBL and carbapenemase encoding genes by the PCR assay.

Results: The highest and lowest resistance rates were observed against ampicillin (93.3%) and tigecycline (9.3%), respectively. Based on the results of phenotypic tests, 46.7% and 25.3% were positive for ESBL and carbapenemase enzymes, respectively. In addition, using the molecular method, the predominant ESBL-, and carbapenemase-associated genes were blaTEM (34.3%) and blaOXA-48 (57.8%), respectively.

Conclusion: Based on the study, it has been found that K. pneumoniae strains produce significant rates of beta-lactamase enzymes, which is extremely alarming. As carbapenem resistance is an alarming public health issue, early detection of the isolates and effective infection control measures are necessary to prevent their further spreading.

Keywords: Klebsiella pneumoniae, Antibiotic resistance, Carbapenemase, MHT

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Pioneering the Application of Nanotechnology in Enhancing Fertility Treatments: A Novel Approach in Women's Reproductive Health (Review)

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Introduction: The sphere of Women's Reproductive Health, particularly fertility treatments, is shifting under the influence of nanotechnology. While conventional therapy approaches deliver mixed results, primarily due to biological complexities and safety concerns, nanotechnology is carving a promising path for significant breakthroughs in fertility treatments. This emerging field could be revolutionary due to the unique properties of nanoparticles, like their reactive nature and high surface-to-volume ratio, which are crucial for effective drug delivery systems capable of surpassing biological barriers, such as the placental barrier.

Methods: In this review, studies detailing the practical implications of nanotechnology, its engagement in medicine, particularly in treating placental dysfunction and infertility, were critically examined. Examining such a wide array of source data enabled us to offer a holistic insight into nanotechnology's application in fertility enhancement. Key factors analyzed involved the physical, chemical, biological, and functional properties of nanoparticles, focusing on their potential as targeted drug delivery systems to treat reproductive health issues.

Results: The collected reports and analyses reflect an encouraging potential for nanotechnology to transform fertility treatments. The nanoparticles exhibited promising characteristics for biomedical applications, including size and conformation, which are instrumental in determining their trajectory dynamics. More importantly, nanoparticles exhibited an impressive ability to deliver therapeutic agents with precision, reducing associated risks to mothers and fetuses. Other minimized risks include adverse drug reactions and organ toxicity, given the targeted action of nanoparticles.

Conclusion: Indeed, nanotechnology stands as a beacon of hope in dealing with complex reproductive health issues. It combines the principles of biology,

physics, and chemistry in an innovative way to improve fertility treatments. However, this revolutionizing field still necessitates further exploration, evaluation and clinical trials to establish optimal nanoparticles for safe and effective application in fertility treatments. The small-scale success stories of nanomedicinal applications provide a strong foundation and build a promising picture of nanotechnology's role in enhancing fertility treatments, presenting novel pathways in Women's Reproductive Health.

Keywords: Nanotechnology Fertility treatments Women's reproductive health Nanoparticles Targeted drug delivery

Plant derived Extracellular vesicles (EVs) and biomedical : engineering, applications and achievements (Review)

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Introduction: Natural plants have attracted increasing attention in biomedical research due to their countless benefits. Extracellular vesicles (EVs), some plant components, are heterogeneous, spherical, or nano-sized cup-like vesicles released by almost all eukaryotes and prokaryotes. cells. EVs are rich in bioactive substances such as metabolites, proteins, lipids, RNAs, miRNAs, mRNAs, and DNA, and can deliver their cargo to recipient cells and play an essential role as extracellular messengers in cellular communication. perform In the field of EVs research, there are five methods that have been used to isolate and purify these vesicles. These methods include ultracentrifuge methods, separation techniques based on exosome size, sedimentation techniques, immunoblotting techniques, in addition to microfluidic techniques. EVs have a phospholipid bilayer decorated with functional molecules and an encapsulated parent matrix, which has attracted interest in the development of designer/hybrid engineered exosome nanocarriers. The structural versatility of EVs allows their original configuration to be modified using various methods, including genetic engineering, chemical methods, physical techniques, and microfluidic technology, to load exosomes with additional cargoes for broad biomedical applications. , correct Exosomes show great potential to overcome the limitations of conventional nanoparticle-based techniques in targeted therapy. Many studies have shown that the properties of plant-derived nanoparticles are similar to those of mammalian exosomes. Propagation of plant EVs has recently become a topic of interest regarding the possibility of intercellular communication, even between different species. A large body of evidence shows that plant EVs can be absorbed in the mammalian gastrointestinal tract and have the potential to mediate plant-animal cell communication. They also hold promise for treating diseases, and their vesicular structure makes them suitable carriers for drug delivery and enables large-scale production. Studies have shown that plant-derived EVs play an important role in tumor suppression. These nanovesicles are effective in cancer treatment by

selectively activating tumor cell apoptosis, regulating inflammatory factors, modulating the tumor microenvironment, and providing therapeutic agents. In addition, they can regulate the tumor microenvironment by stimulating the polarization of tumor-associated macrophages (TAM) towards the M1 phenotype and facilitate the inhibition of cancer cell growth. Extracellular vesicles have potential importance in gastrointestinal diseases. Studies have shown that EVs can persist in digestive environments because they resist digestion by various enzymes such as intestinal pepsin and pancreatin and have a more therapeutic role. For example, ginger-derived ELNs (GELNs) alter the composition of the microbiome and have a positive effect on host physiology. EVs isolated from plants such as soybean, ginger, hamilon, grapefruit, tomato, and pear contain micro RNA (miRNA) that can target human transcripts. For example, Zhou et al showed that honeysuckle-derived exosomes contain miR-2911, which can bind to 28 binding sites in the SARS-CoV-2 genome and inhibit virus replication. EVs can cross various physiological barriers, including the blood-brain barrier, through receptor-mediated cell transport and membrane fusion, and act as drug carriers. For example, grapefruit-derived EVs can precisely transport doxorubicin to the tumor site and lead to improved anti-glioma effect. Research has shown that electric cars also have cardioprotective effects. In one study, Liu et al found that exosomes derived from ginseng root could reduce doxorubicin-induced H9C2 heart damage by protecting mitochondrial apoptotic pathways. Also, blueberry-derived EVs (B-ELNs) prevent damage caused by various stressors to the vascular system by regulating the expression of genes induced by TNF-α and reducing the production of reactive oxygen species (ROS). Therefore, this article briefly states that PEN components including lipids, proteins, genetic material and active small molecules have a high potential in maintaining environmental homeostasis and preventing various diseases. Considering that there are simple techniques for isolation, purification and identification of different PENs, vesicles of natural plant origin can provide a theoretical basis for their development and better use with an important role in the human health industry and beyond.

Methods: literature review

Results: literature review

Conclusion: Since their discovery, plant EVs have shown very good performance in the fields of biological therapy, drug delivery, and crossing biological barriers, and have attracted the attention of more and more experts and researchers, and gradually gained new popularity in the fields of have become different. Although EVs were discovered at an early stage, compared

to mammalian and human vesicles, they have not been fully studied, especially in tissue engineering and biomedicine, where they are more at the in vitro research stage. At present, the isolation and purification of EVs is relatively simple, the extraction process is less optimized, and yield and purity are still prerequisites for the realization of clinical development of plant vesicles. Plant vesicles have shown excellent performance in drug delivery, including the delivery of insoluble drugs such as curcumin, DOX, folic acid, and miRNAs, as well as large molecule drugs. Recent evidence suggests that the use of nanoscale particles, such as exosomes, in cancer immunotherapy could pave the way for the development of new cancer vaccines through antigen-presenting cell technologies that prime the immune system to recognize and kill cancer cells. . Combined with nanotechnology, engineered exosomes are becoming a new approach to cancer vaccine development. The biosafety of EVs is superior to other nanoparticles and they are promising nanocarriers for clinical use, making them attractive candidates for cancer vaccine development. For food applications, the phospholipid bilayer of EVs protects the vesicle structure and its contents from the gastrointestinal tract and gastric acid environment, thereby ensuring their stability. EVs can effectively reduce inflammatory bowel disease and customize personalized mixed drinks for patients, which has a special application prospect in food development. In bioengineering, gene editing has become a powerful therapeutic technique, but the lack of safe and effective in vivo delivery systems has limited its widespread clinical application. With the advancement and optimization of gene editing tools, the continued development of exosome-based delivery systems provides an impetus for targeted gene therapy. Despite the success of plant vesicles, developing plant vesicles still faces challenges. More innovations and advances are needed to overcome these challenges and accelerate the clinical translation of plant vesicles.

Keywords: Plant EVs, biological therapy, Engineering, Nanotechnology

Platelet microparticle; a potential targeted drug delivery system (Review)

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Introduction: Along with undeniable advantages, systemic administration of chemical drugs may accompany severe toxicity and side effects due to adverse reactions with normal cells. The ideal situation for disease treatment is to transport drugs directly to the target organs, tissues, cells, and even specific organelles. Although several drug delivery systems such as liposomes and different synthetic nanoparticles have been identified, their clinical application is crippled by high costs and limited biological adaptability. Therefore, the development of new systems seems to be crucial. Platelets are anucleated cells with the main activity in the coagulation system. Activation of platelets in physiological or pathological circumstances leads to the formation of platelet microparticles (PMPs). PMPs, extracellular fragments secreted by activated platelets, range in size from 0.1 to 1 μm in diameter. PMPs account for more than 70% of circulating microparticles. PMPs are safe, inexpensive, and biocompatible particles that have the capacity to carry drugs. The presence of platelet membrane antigens on PMPs covers them against the phagocytic system and prolongs their half-life in comparison with other microparticles. Besides, autologous PMPs may be applicable to prevent adverse transfusion reactions. The present study aims to overview the application of PMPs as a specified drug delivery system in a variety of diseases.

Methods: A literature search was done in Web of Science, PubMed, and Scopus using related keywords such as platelet microparticles, platelet extra-cellular vesicles, platelet-derived microparticles, platelet-derived extracellular microvesicles, drug delivery system, target therapy, etc. No time, language, or article type restriction was performed. An additional manual search of the references of related articles was also conducted.

Results: To date, isolating PMPs and loading drugs are known as the major complications of using PMPs as a drug delivery system. Although some studies suggest incubation instead of sonication and freeze-thaw for loading drugs in PMPs, lacking a single standard protocol results in variable outcomes. In recent years, there have been great advances in loading different therapeutic agents on PMPs. For instance, promising effects for

loading antivirals such as Lamivudine and Tenofovir disoproxil fumarate have been documented using different cell lines. In addition, anti-tumor agents were also tested. For example, Kailashiya et al. (2019) reported that Doxorubicin (DOX) loaded PMPs showed much greater toxicity compared with the equivalent dose of free DOX. They also revealed that incubation of cancer cells with PMP-DOX for an hour resulted in 7 times higher drug uptake than those incubated with DOX alone.

Conclusion: Previous studies prepared preliminary insights into drug-loaded PMPs and suggested that drug-loaded PMPs may be clinically applicable in the near future. However, the Mechanisms by which PMPs transport drugs to different cells are yet to be fully understood. In addition, further in-vitro and in-vivo studies are needed to realize the effects of drug-loaded PMPs in other diseases. Possible adverse effects including procoagulant activities of PMPs are also still unclear.

Keywords: targeted therapy, drug-delivery vector, platelet microparticles, treatment, synthetic nanoparticles

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Polycaprolactone/multiwall carbon nanotube/ellagic acid-loaded liposome scaffold containing mesenchymal stem cells as a novel platform for improved tissue regeneration (Research Paper)

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2.
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Introduction: The efficiency of an engineered scaffold in regenerating damaged tissue could be enhanced by stem cell seeding and drug loading. The aim of the present study is to establish a platform of scaffold, drug and stem cells for tissue engineering applications.

Methods: The composite scaffolds were synthesized by electrospinning of PCL/functionalized multi-walled carbon nanotube (f-MWCNTs) composite followed by ellagic acid (EA) liposomes loading, and adipose-derived mesenchymal stem cells (ADMSCs) seeding.

Results: Transmission electron microscopy revealed that f-MWCNTs were well-aligned along nanofibers. Beadles fibers and fine distribution of nanoliposomes on the surface of the composite scaffold were observed by scanning electron microscopy. Ultimate tensile strength, elongation at break and Young's modulus were obtained at 3.37 MPA, 61%, and 15 MPa, respectively, for the composite scaffold. The scaffold showed 27% of weight loss after 56 days. UV-Vis spectroscopy demonstrated 70% of ellagic acid release after 168 h. EA-loaded liposome dramatically enhanced the hydrophilicity of scaffolds. The MTT assay, DAPI staining, acridine orange/ethidium bromide staining, and FE-SEM images displayed the favorable seeding, proliferation, adhesion and survival of the ADMSCs on the platform.

Conclusion: Overall, the results suggested that a combination of ADMSCs seeding on PCL/f-MWCNT scaffolds covered with EA-loaded liposome has potential for tissue regeneration applications.

Keywords: Fibrous scaffold, PCL, Modified multiwall carbon nanotube, Drug delivery, Adipose derived stem cells

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polycystic ovary syndrome disease review article (Review)

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Introduction: pcos patients are not always markedly overweight but pcos is stongly associated with abdominal obesity and insulin resistance. effective approashes to nutrition and excercise improve endocrine features, reproductive function and cardiometabolic risk profile. even without marked weight loss, recent studies allow us to make recommendations on macronutrient intake.

Methods: polycystic ovary syndrome (pcos) and hyperprolactinemia (HPRL) are the two most common etiologies of anovulation in women. pcos or polycystic ovary syndrome is a common endocrine disorder that occurs during the reproductive age females. it manifests in the form of a wide range of symptoms including (but not limited to) hirsutism, amenorrhea, oligomenorrhea, obesity, acne vulgaris, infertility, alopecia and insulin resistance. the incidence of depression in pcos population is increasing as compared to the general population.

Results: previous studies have found that there are specific changes in the intestinal flora of p c s patients, and interventions to modify the intestinal flora can significantly improve the symptoms of pcos. women with pcos have a higher incidence of vaginitis compared to healthy women. few studies to- date have focused on investigating vaginal flora.

Conclusion: during pregnancy, gestational diabetes. and gestational hypertensive disorders can occur. at an older age, metabolic disease such as glucose intolerance, type2 diabetes or dyslipidaemia are frequently described. women with pcos have increased classical cardiovascular risks and increased subclinical cardio-vascular disease without proven increase of cardiovascular morbidity and mortality.

Keywords: resistance , ovary , Pco , syndrome

POSSIBLE ANTIDIABETIC EFFECTS OF URTICA DIOICA HYDROALCOHOLIC EXTRACT AND MOLYBDENUM DISULFIDE NANOPARTICLES ON STREPTOZOCINE INDUCED PANCREATIC CELL LINE (Research Paper)

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Introduction: Diabetes Mellitus is known as a chronic metabolic disorder and it is characterized by hyperglycemia which could be caused by deficiency of insulin secretion, insulin action, or both. Among various types of diabetes, type 1 DM (T1DM) and type 2 DM (T2DM) are the most usually discussed. T1DM is also known as insulin-dependent diabetes. It is primarily due to pancreatic islet beta cell destruction and it leads to deficiency in insulin production in the body. While T1DM cannot be prevented with current knowledge, T2DM can be prevented as well as treated easily, since management of diabetes is complex, it should include a healthy diet and lifestyle. Nowadays, available therapies for diabetes include insulin and various oral antidiabetic agents, although they have beneficial roles in diabetes control and treatment, they cause unwanted side effects. On the other hand, in developing countries, as products are expensive and not easily accessible. So, using the traditional herbal medicines which are obtained from plants, plays an important role in the management of diabetes mellitus in some areas. Also, scientists show great interest in these plants because of their potential capacity to produce more efficient and safer medicine for diabetic patients. One of the Medicinal Plants with a broad background in the treatment of diabetes is Urtica diouca (UD), which is known as nettle sting. On the other hand, nanotechnology has emerged as a new promising agent in the treatment of various diseases such as Alzheimer's and different types of cancers.

Methods: In this in vitro study we aimed to investigate the possible antidiabetic effects and Biocompatibility of molybdenum disulfide nanoparticles (MoS2 NPs), one of the less investigated two-dimensional metal nanomaterials, in living cellular environments. The pancreatic beta cell line (RIN-5F) was induced by streptozocine in order to intimate cell’s condition under diabetes stress. At first, the optimal concentration of UD hydro alcoholic extract and MoS2NPs were obtained by MTT test. Then, in the second phase of the study, insulin concentrations in the cell culture medium were measured by ELISA kit. The expression of some glucose metabolism-related genes like

GCK, GLUT2, INS were also determined. In order to study the possible cytoprotective effect of the agents, BCl2 gene expression was measured too.

Results: According to our results, MoS2 NPs and UD hydroalcholic extract concentrations show increases in insulin secreting levels individually and synergic. And they show improved effects on some glucose metabolism-related genes like GCK,GLUT2,INS and apoptotic genes like BCL.

Conclusion: In conclusion, defined concentration of MoS2 NPs and UD hydroalcholic extract can show synergic cytoprotective effects and antidiabetic effects on some of the parameters but have antagonistic effects on others.

Keywords: diabetes, molybdenum disulfide nanoparticles, Urtica diouca, diabetes management, genes expression

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Post-Covid 19 Consequences on the Physical, Mental, and Social Well-being of Post-covid Patients, Mechanism of Complications, and Strategies for Prevention (Review)

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Introduction: People who have recovered from covid-19 but are still reporting long-term consequences of the illness are referred to as having "long covid." This review will collect pre-existing literature and summarize the outcomes of Covid-19 on the physical, mental, and social well-being of post-covid patients, the mechanism of these complications, and potential prevention strategies.

Methods: The studies have been identified through PubMed searches based on WHO definition of health and well-being.

Results: According to the research articles, in terms of Physical health, multiple organ systems showed various complications. In the mental health, many patients reported a significant decline in mental health. The Covid-19 pandemic has also altered how people connect with one another particularly in terms of social health. The pathophysiology of physical health dysfunction is said to be of multifactorial etiology, whereas in terms of mental health, the unpredictable nature of the COVID-19 pandemic, lockdown and economic collapse that followed and social health complication post-COVID-19 situation is seen because the social support typically received had been significantly disrupted.

Conclusion: The physical, mental, and social wellbeing of patients have been disrupted by prior Covid-19, according to numerous findings that had been published. We may have more unforeseen issues as time goes on as a result of this pandemic. It is imperative to fully understand COVID-19's long-term implications on health in order to enhance each survivor's quality of life. This

will make it possible to provide preventive measures for physical, mental, and social health in a responsible and timely manner.

Keywords: Health, Post-Covid, Complications, Management, Prevention

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Potential of Fucoidan in the Treatment of Osteoporosis: A Systematic review (Review)

Robab Bahreini,[1,*] Elham Sasan,[2] Haniye Fazli,[3] Niloofar Dehghan,[4] Neda Baghban,[5]

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Introduction: Osteoporosis is a common skeletal disorder that results in decreased bone density and increased risk of fractures. Fucoidan, a sulfated polysaccharide found in brown seaweed, has been suggested as a potential treatment for osteoporosis due to its ability to regulate bone metabolism and regeneration. The aim of this systematic review is to evaluate the existing evidence on the potential of fucoidan in the treatment of osteoporosis.

Methods: A comprehensive search was conducted using PubMed database from inception until May 2023. Studies that investigated the effects of fucoidan on osteopetrosis in animal models or in vitro were included. The keywords were (Fucoidan[Title/Abstract]) AND ((osteogenic[Title/Abstract]) or (Osteoporosis[Title/Abstract]) or (bone[Title/Abstract]) or (Osteogenesis[Title/Abstract])).

Results: A total 90 studies were included in this review including in vitro, animal, and human studies. In vitro and animal studies showed that fucoidan had a positive effect on bone health by increasing osteoblast differentiation and mineralization and decreasing osteoclast differentiation and activity. Human studies showed mixed results, with some studies reporting a positive effect of fucoidan on bone density and others reporting no significant effect.

Conclusion: Fucoidan has potential as a therapeutic agent for the treatment of osteoporosis. Further studies are required to investigate the safety and efficacy of fucoidan in human subjects with osteoporosis. Fucoidan may represent a promising alternative or complementary therapy for osteoporosis, but more research is needed to establish its role in clinical practice.

Keywords: fucoidan, Osteoporosis, bone, osteogenesis, differentiation.

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Preconditioning with SDF-1 improves therapeutic outcomes of bone-marrow-derived mesenchymal stromal cells in a mouse model of STZ-induced diabetes (Research Paper)

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Introduction: Numerous experimental studies have suggested that bone marrow mesenchymal stem cells (BMMSCs) ameliorate diabetes in animal models. But a number of critical obstacles lie ahead of this new strategy including reducing stem cell homing to the damaged tissue. The present study to investigate whether preconditioning of BMMSCs with stromal derived factor 1α (SDF-1α) could enhance their homing to the pancreas and promote regeneration of the pancreatic β cells after being intravenously injected.

Methods: The BMMSCs were isolated by flushing method and identification of the cells was done by flow cytometry for CD73+, CD90+, CD34- and CD45- markers. On 10 days after STZ induction of diabetes, BMMSCs or BMMSCs+SDF1α at a dose of 1×106 cells/1 ml PBS were transplanted via the tail vein. The same volume of PBS (1 ml) was injected as a vehicle. 48 hours after transplantation, homing of BMMSCs were analysis by flow cytometry and fluorescent microscope. At 30 days after the cell transplantation, blood and pancreatic tissue samples were taken from all mice for biochemical and histological studies.

Results: BMMSCs+SDF-1α had a high ability of homing into the injured pancreas ($P \leq 0.05$ vs. BMMSCs). The BMMSCs+SDF-1α group showed further differentiation into insulin secreting βcells ($P \leq 0.05$ vs. BMMSCs). Transplantation of BMMSCs+SDF-1α significantly reduced blood glucose level ($P \leq 0.05$ vs. BMMSCs).

Conclusion: Our results showed the effectiveness of SDF-1 preconditioning in BMMSCs transplantation of STZ-induced diabetes mice, might be achieved through improvement of BMMSCs homing into the injured pancreas.

Keywords: Diabetes mellitus; Transplantation; bone marrow mesenchymal stem cells; stromal derived factor 1α

Predicting Glioblastoma-Associated MicroRNAs Through Bioinformatics Analysis (Research Paper)

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Introduction: Predicting various microRNAs associated with glioblastoma through bioinformatic approaches is a critical research area in cancer biology and bioinformatics. Glioblastoma, a highly aggressive form of brain cancer, presents significant challenges in terms of diagnosis and treatment. MicroRNAs (miRNAs) are short RNA molecules that play crucial roles in gene regulation and have been implicated in the development and progression of glioblastoma. This research aims to leverage the power of bioinformatics tools and techniques to analyze genomic and transcriptomic data. These dysregulated miRNAs may serve as biomarkers for early diagnosis or therapeutic targets for this deadly disease. Recent advancements in high-throughput sequencing technologies have generated vast amounts of data, making bioinformatic analysis an indispensable tool for uncovering the intricate molecular mechanisms underlying glioblastoma. This approach not only enhances our understanding of the disease but also offers new avenues for the development of personalized treatment strategies. The integration of multidisciplinary knowledge from genetics, bioinformatics, and oncology is crucial for making strides in glioblastoma research.

Methods: The expression profiles of glioblastoma-related genes were assessed in the GSE100675 dataset using the GEO2R package from the Gene Expression Omnibus (GEO).To pinpoint the most significant genes contributing to glioblastoma onset, we conducted differential expression analysis and further examined these genes in the DAVID database.In parallel, we identified microRNAs associated with these critical genes using the miRWalk database.The Human microRNA Disease Database (HMDD) was instrumental in revealing the microRNAs implicated in glioblastoma pathogenesis.

Results: The analyses revealed the significant role of the myelin transcription factor 1-like (MYT1L) gene in glioblastoma.Utilizing the miRWalk database, we identified a set of MYT1L-related microRNAs, including hsa-miR-21-3p, hsa-miR-10a-5p, hsa-miR-15a-5p, and hsa-miR-19b-3p.

Conclusion: Using bioinformatics to predict microRNAs associated with glioblastoma holds promise for improving our understanding of this aggressive

brain cancer. These microRNAs could serve as vital diagnostic tools and potential therapeutic targets. The interdisciplinary approach of genetics, bioinformatics, and oncology is pivotal in advancing glioblastoma research. This innovative use of computational techniques offers hope for more effective treatments and better outcomes in the battle against glioblastoma.

Keywords: Glioblastoma, Bioinformatics, MicroRNA, Prediction

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Predicting the interaction of miR-122-5p and EZH2 in liver cancer through bioinformatics analysis (Research Paper)

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3.

Introduction: Primary liver cancer is the second leading cause of cancer-related death worldwide and therefore a major public health challenge. Primary liver cancer comprises hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA), and other rare tumors, notably fibrolamellar carcinoma and hepatoblastoma (1). Liver is the major metabolic center for both carbohydrate and lipid, thereby maintaining glucose homeostasis (2). With the advances in high-throughput profiling techniques and the availability of public data sets such as The Cancer Genome Atlas Program (TCGA), a broad range of coding transcripts have been profiled and their underlying modes of action have been mapped(3).mir122-5p has unique potential as a prognostic biomarker in liver cancer. Mir 122-5p has significantly increased expression in Liver cancer tumor tissue (4). The regulation of many pathways in cell biology is regulated by miRNAs. Obtaining miRNA target genes is effective for negative regulation of this pathways and can also help to understand the regulatory mechanism and gene therapy of cancer. The EZH2 gene, which is expressed in various solid tumors, including liver cancer, can regulate gene transcription and promote the generation and progression of tumors. Our aim was to investigate the relationship between EZH2 and multidrug-resistance of human hepatic cancer cells using RNA interference (5).

Methods: In this project, after miRNA target gene prediction by mirwalk database, we analyzed TCGA RNA-seq data and predicted gene expression patterns.

Results: The results showed that EZH2 with a high score in the CDS is targeted by miR-122-5p. Also, the results of TCGA data analysis showed that the expression level of this gene in Liver cancer tumor tissue was significantly Increase.

Conclusion: Predictions showed that increasing the expression of miR-122-5p causes a decrease in EZH2 expression in liver cancer. It is also predicted that the increase in the expression of EZH2, in addition to the role of a biomarker in the diagnosis of liver cancer, can be a factor in the development of liver cancer and the activation of the pathway.

Keywords: Key word: liver, cancer, has-miR-122-5p

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Prenatal Stem Cells: A Promising Resource for Craniofacial Bone Tissue Engineering (Review)

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Introduction: The articles explore the potential application of perinatal stem cells in tissue engineering for the regeneration of craniofacial bone. Recent improvements in tissue regeneration in bone defects demonstrate the limits of existing techniques used to restore cranial bone abnormalities and highlight the need for novel stem cell-based procedures. This article talks about three types of stem cells: adult mesenchymal stem cells (MSCs), embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs). All of these stem cells can create bones. These sources, however, have their own drawbacks, such as scarcity, invasive obtaining methods, and concerns about ethics. Such stem cells are a promising source for tissue engineering as they have unique features. They have properties identical to adult stem cells and ESCs, show immunoprivileged status, and have an extensive range of multipotent plasticity.

Methods: Breakthroughs and issues regarding stem cell-based craniofacial bone reconstruction are discussed by the researchers. Perinatal stem cells have many advantages. These advantages include their large quantity, ability to multiply, and capability to transform into different types of cells. These characteristics are currently being highlighted because of their potential in regenerating craniofacial bone tissue.

Results: In conclusion, perinatal stem cells hold great promise for extensive use in craniofacial bone tissue engineering. Scientists suggest that with further research and development, perinatal stem cell-based strategies can be applied for customized and functional clinical reconstruction of craniofacial bone defects.

Conclusion: Perinatal stem cells are commonly seen as a practical and viable option for allogeneic transplantation This is mainly due to their low immunogenicity and their significant potential to affect the immune system.

Keywords: Stem cells, Tissue engineering ,Bone tissue ,Craniofacial bone regeneration ,Perinatal stem cells

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Prevalence and antimicrobial resistance of Shigella species isolated from diarrheal patients in tehran, Iran (Research Paper)

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Introduction: shigellosis is a significant global human health problem, and shigella is in charge of almost 165 million cases of this disease annually, of whom 163 million cases are in developing countries. the main aims of the current study were to identify shigella spp. isolated from diarrheal patients and determination its antimicrobial susceptibility.

Methods: the bacterial isolated were identified as shigella spp. by microbiological tests and were serotype by the slide agglutination test. antimicrobial susceptibility testing was performed using the disk diffusion method. PCR was performed to detect the ipaH gene.

Results: the shigella strains were isolated from 250 patients with various diarrhea, including bloody diarrhea (5%), mucoid plus bloody diarrhea (2%), mucoid diarrhea (4%), and watery diarrhea (3%). overall, 88 (35.2%) isolated were positive for shigella spp., of which 39 (44.31%) serotypes were identified as shigella flexeneri, 26 (29.54%) serotypes were identified as shigella sonnei, 15 (17.04%) serotypes were identified as shigella dysenteriae, and 8 (9.09%) serotypes were identified as shigella boydii. antibiotic susceptibility test revealed that the highest resistance percentage was related to trimethoprim-sulfamethoxazole (68%), and ciprofloxacin and cefixime were the best antibiotics against shigella isolates.

Conclusion: we concluded that shigella spp. can be considered as an etiology agent of diarrhea in Southwest Iran. since the drug resistance pattern of Shigella differs geographically and over time within a country, continuous and regular surveillance program is necessary.

Keywords: shigella, diarrhea, antimicrobial resistance, Iran

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Prevalence of Demodex folliculorum infection in patients referred to the Dermatology Clinic of Imam Reza Hospital in Tehran in 2019 (Research Paper)

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Introduction: One type of external human parasite is worm-shaped scabies called Demodex. Demodex folliculorum and Demodex brevis live in the hair follicles and sebaceous glands of human skin and various mammals, respectively. The mentioned infection should be studied from various clinical and epidemiological aspects in Iran. Therefore, this study was designed and conducted to investigate the frequency of D. folliculorum infection in patients referred to the Dermatology Clinic of Imam Reza Hospital in Tehran.

Methods: Patients with symptoms and skin lesions such as rosacea, skin redness, itching, burning, scaling, and pustules were selected as the study group. After obtaining written informed consent from the subjects and providing the necessary explanations, the research questionnaire was completed to provide background information including age, education, employment status, history of skin diseases, and marital status. To test for Demodex contamination, surface skin chips were prepared, and the samples were taken to the laboratory for testing. Some of the skin chips were placed on a clean microscope slide and clarified by adding a drop of 10% potash solution to one slide and a lactophenol solution to the other. After placing the other slide on top of the sample slide, microscopic observation was performed using objective lenses with magnifications of 10, 4, and 40 times. Demodex-positive cases were photographed at the prepared magnifications and identified by comparing the morphological features and parameters described in the valid sources.

Results: In this study, 100 patients referred to the Dermatology Clinic of Imam Reza Hospital in Tehran with clinical suspicion of infection as diagnosed by a dermatologist, were randomly included in the study. The mean age (standard deviation) of the patients was 26.81 (7.23) years.

Regarding gender, 57% of the patients were female and 43% were male. The highest level of education was masters and bachelors (48%) and most of the patients were students and employees. Overall, 10% of patients had a history of skin disease (eczema/hives/fungal infection) and 7% of patients had taken antibiotics in the previous two months. In addition, 3% of patients had an underlying disease (blood pressure/CVA/diabetes). The most common skin manifestations were acne (85%), rosacea (11%) and blepharitis (4%). On examination, Demodex was positive in 6 cases (6%), with 4 cases of mild and 2 cases of moderate involvement. This study investigated the frequency distribution of Demodex infection in patients according to sex, age, education level, skin manifestations, history of skin disease, underlying disease, history of antibiotic use, marital status, and occupation. Among these, only the relationship between Demodex infection and history of skin disease was statistically significant, such that half of the infected patients had a history of skin disease.

Conclusion: The current study showed that compared with other studies, the prevalence of D. folliculorum infection is much lower and is about 6% in patients with suspicious symptoms, and on the other hand, according to the current study, infection with this parasite is only related to the positive history of skin disease and no significant relationship with other variables was observed.

Keywords: Demodex folliculorum, Infection, Skin lesions.

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Prevalence of factors causing urinary tract infection in patients referred to khatam ol anbiya hospital the city of Shirvan in 2022 (Research Paper)

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Introduction: Urinary tract infection (UTI) is one of the most common causes of bacterial infection in the community and hospital. Urinary tract infection is more common in women than in men .The economic and public health costs resulting from urinary tract infection and the increasing antibiotic resistance are significant and have a large impact on the quality of life of infected patients .

Methods: In this descriptive-cross-sectional study, during a one-year period from April to March 2022, urine samples of outpatients and inpatients referred to khatam ol anbiya hospital in Shirvan were collected using the Clean Catch Midstem method. First, the samples were cultured on Mc Conkey agar and blood agar media, and incubated at 35-37°C for 24-48 hours. A colonization rate equal to or greater than 105 colonies per ml was considered as a positive sample. Then the morphology of the colonies is examined and standard biochemical tests are carried out in cluding: Urea, SIM, MR/VP, TSI and Simon Citrate, phenylalanine deaminase and warm dyeing were used.

Results: In this study, 1096 urine samples from outpatients and inpatients referred to the laboratory of khatam ol anbiya Shirvan Hospital, 119 urine cultures (10.85%) were positive 86 samples (72.27%) are women and 33 samples (27.73%) are men. The most common bacterial isolate is Escherichia coli with 52 (43.7%), Candida sp 29 (24.36%), Enterococcus 14(11.76%) Klebsiella species with 8 (6.73%%), Staphylococcus epidermidis 8 (6.73%), Pseudomonas aeruginosa 5 (4.20%), Non-Enterococcus 2 (1.68%), Staphylococcus aureus 1(0.84%) were isolated.

Conclusion: According to the obtained results, Escherichia coli bacteria is the most common cause of urinary infection, which is more than other isolates and is the most dominant bacteria in causing urinary infection. Candida sp is the second cause of infection, which has a significant difference compared to other Gram-negative and Gram-positive bacteria.

Keywords: Urinary tract infection, shirvan, Bacterial isolates

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Prevalence of integrons and ESBL genes and their relationship with FimH gene in multidrug resistant uropathogenic Escherichia coli isolates from urinary tract infections (Review)

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Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections globally, influencing 150 million individuals every year around the world. Uropathogenic Escherichia coli (UPEC) is the most common causative agent of UTI. Emergence of multidrug-resistant isolates is the caused by excessive and inappropriate use of antibiotics. UPEC generally use various adhesins to binding and invading bladder cell. Type 1 fimbriae (FimH) is one of the most common fimbriae appear to play a role in inter-bacterial binding and biofilm formation. In fact biofilm formation seems provides an promoted growth and persistence of bacteria resulting in resistance to antibiotics.

Methods: Integrons are mobile genetic elements play that important role in the development of antibiotic-resistance strains. On the other hand, extended-spectrum beta lactamase (ESBL) are a group of enzymes that usually resistant to various antibiotics. The ESBL genes can be carried by integron-containing isolates to make them multidrug resistance. The prevalence of class 1, 2, 3 integrons and ESBL genes and fimH gene was verified by the PCR method. Antimicrobial susceptibility of UPEC isolates was performed using disc diffusion method. biofilm formation was investigated using microplate method. The findings indicated that MDR and non MDR isolates tended respectively to form weak and strong biofilms, formation. A high prevalence of fimH and PAP genes was found. In strains that were resistant to ampicillin, a significant correlate with biofilm producers was present. Another study showed that there was no significant reduction in biofilm in ampicillin sensitive strains. Antibiotic susceptibility testing showed that resistance among ESBLs producers was significantly higher than non-ESBLs producers.

Results: The prevalence of integrons and ESBLs are remarkably associated with resistance to used antibiotics. These findings indicated that the significant between MDR phenotype and the potential for biofilm formation will lead to

relapse of infection. Therefore, more investigations can be effective on the treatment of antibiotic resistance.

Conclusion: Moreover there was a significant correlation between ciprofloxacin and reduction in biofilm biomass.

Keywords: UTI, Escherichia coli, biofilm, integron, MDR

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Prevalence of oxacillin-susceptible and methicillin-resistant Staphylococcus aureus strains isolated from healthy carriers in Ardabil, Iran (Research Paper)

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Introduction: Methicillin-resistant Staphylococcus aureus (MRSA) is often the cause of a wide broad of infections ranging from minor skin infections to serious infections such as toxic shock syndrome (TSS) in hospital and community settings.

Methods: 200 nasal swab samples were randomly collected from male and female students at three different high schools in Ardabil, Iran. After confirmation of S. aureus strains by standard biochemical tests, the antibiotic sensitivity pattern of the isolates was determined by the disk diffusion method. The presence of the mec A gene was examined by PCR.

Results: From 250 students, 14.4% (n = 36) were positive for S. aureus. Antimicrobial susceptibility testing was performed using 12 antibiotic disks. Based on the results, 100% of the isolates were resistant to ampicillin while all were sensitive to vancomycin. Moreover, 16.66% of S. aureus isolates were resistant to cefoxitin and 8.33% to oxacillin. The presence of the mec A gene was confirmed in 50% of cases. These results indicated oxacillin-susceptible mec A-positive S. aureus (OS-MRSA) colonization among students.

Conclusion: Our findings highlight the spread of OS-MRSA among the healthy population in Ardabil, Iran. Genetic and phenotypic tests are needed to accurately detect MRSA.

Keywords: Staphylococcus aureus; MRSA; mec A; School students

Probiotics and their Role in Mitigating Cognitive Decline (Review)

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Introduction: The gut microbiota, a group of microorganisms residing in our intestines is now acknowledged as playing a crucial role in promoting our general well-being. Within this community, probiotics refer to bacteria and yeasts that particularly support the digestive system. Recent studies have started to suggest a connection, between these gut microorganisms and our brain leading to the notion of the gut-brain axis.

Methods: The Gut-Brain Axis The gut-brain axis is about the two-way communication between the central nervous system and the enteric nervous system. Recent research indicates that our gut microbiota can influence this axis, which in turn can affect our brain function and behavior. Scientists believe that this impact is caused by factors, such, as the vagus nerve, immune system, gut hormones, and microbial metabolites. Probiotics and Cognitive Health Recent studies are suggesting that alterations in the gut microbiota composition and function can influence neurodevelopment, cognition, mood, and behavior). Dysbiosis or imbalance in the gut microbiota has been associated with a variety of neurological and psychiatric disorders, including Alzheimer's disease, Parkinson's disease, depression, and autism spectrum disorde. Therefore, strategies aiming to correct dysbiosis, such as the use of probiotics, are being explored for their potential therapeutic benefits. Several studies have reported beneficial effects of probiotics on cognitive function. For example, a randomized, double-blind, controlled clinical trial found that a 12-week intervention with a probiotic mix (Lactobacillus and Bifidobacterium strains) improved cognitive function in patients with Alzheimer's disease. Another 12-week randomized controlled trial showed that daily consumption of a fermented milk product containing four probiotic strains could beneficially alter brain activity in healthy women.

Results: Potential Mechanisms The exact mechanisms by which probiotics may exert their beneficial effects on cognitive function are not yet fully understood. However, several potential mechanisms have been proposed. One theory is that probiotics may modulate the immune system, reducing the systemic inflammation that is thought to contribute to cognitive disorders such as Alzheimer's disease. Another theory suggests that probiotics may help maintain the integrity of the blood-brain barrier, which becomes compromised in many neurological disorders. Probiotics may also produce and enhance the

bioavailability of neuroactive substances, such as gamma-aminobutyric acid (GABA), serotonin, and dopamine, which can influence mood and cognition. Furthermore, probiotics might modulate the gut-brain axis by interacting with the enteric nervous system, thereby affecting gastrointestinal motility and secretion, and influencing the sensory and motor functions of the central nervous system.

Conclusion: While the research into probiotics and cognitive decline is still in its early stages, the evidence thus far is promising. Probiotics offer a potentially safe and cost-effective strategy to complement traditional therapies for cognitive disorders. However, more rigorous, large-scale clinical trials are needed to confirm these preliminary findings and to clarify the mechanisms by which probiotics may exert their beneficial effects on the brain. Further research is also required to identify the most effective probiotic strains, as well as the optimal dosage and duration of treatment.

Keywords: Probiotics-Cognition-Gut-Brain Axis-Alzheimer's disease

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Promising nanoparticles and delivery methods to improve Sperm Cryopreservation in assisted reproductive technology (Review)

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Introduction: Sperm cryopreservation (SC) as a crucial stage of assisted reproductive technology (ART) providing long-term storage of samples for procedures such as in vitro fertilization (IVF). Sperm damage can reduce fertility capacity in freeze-thaw process due to crystal formation, stress oxidative and osmatic shock. Glycerol and egg yolk buffer as conventional cryoprotectants may alleviate post-thaw injuries but have limitations. Therefore, nanoparticles emerge as a novel cryoprotective strategy. Various types of nanoparticles such as gold, silica, carbon nanotubes, and graphene have exhibited cryoprotective effects for sperm freezing due to proposed mechanisms include direct membrane stabilization, antioxidant effects, and regulation of apoptosis pathways. These mechanisms improve sperm motility, viability, acrosome integrity, and ATP levels. This is a brief background about potential effect of nanoparticles for sperm post-thaw preservation in ART. This review will provide an overview of current investigations focused on types of nanoparticles, combination and delivery methods in SC to highlight future prospect strategies to optimize the efficacy of SC in ART.

Methods: A comprehensive search strategy was implemented to identify relevant articles on the topic of sperm cryopreservation, nanoparticles and related keywords. Databases including PubMed, Web of Science, Scopus, and Google Scholar were searched for articles published from 2015 to 2023 for identify relevant articles on sperm cryopreservation and nanoparticles. The articles skimmed by two independent reviewers based on title/ abstract. All relevant studies were included. Non-English articles, and other applications of nanoparticles unrelated to cryopreservation were excluded and a flow diagram of the search strategy is listed.

Results: Studies have explored a variety of nanoparticles as novel cryoprotective supplements to improve post-thaw sperm quality in assisted reproduction. gold nanoparticles preserved sperm motility and viability better

than other nanoparticles such as silver, silica, platinum, palladium and magnetic iron oxide. On the other hand, between metal oxide nanoparticles including ZnO, Fe_3O_4, CeO_2, CuO, NiO, and Co_3O_4, investigations found CeO_2 nanoparticles preserved post-thaw sperm motility and viability. Besides, Combinations of nanoparticles demonstrate synergistic benefits. Co-treatment with gold and cerium oxide nanoparticles resulted in improved sperm membrane and DNA integrity after freezing and thawing relative to individual nanoparticles. Silica nanoparticles supplemented with trehalose cryoprotectant better preserved post-thaw human sperm motility and mitochondrial activity compared to trehalose alone. Nowadays, several types of lipid or polymer-based nanoparticles have recently shown promise as sperm cryoprotectants.

Conclusion: Nanoparticles improve the cryopreservation of semen by reducing cytotoxicity and enhancing sperm parameters. Nanoparticles can target physical and physiological characteristics of sperm, such as motility, directionality, apoptosis, and intact acrosome, to predict whether a semen sample is suitable for ART. Incorporating delivery, warming, and washing methods into efficient cryopreservation is also being studied. Overall, the use of nanoparticles in semen cryopreservation is a promising area of research that could lead to improvements in ART success rates. Further optimization of nanoparticle-based freezing extenders may continue enhancing clinical outcomes. However, more investigations are needed to understand the potential benefits and limitations of this approach.

Keywords: Spermatozoa, Cryopreservation, Nanoparticles, Assisted Reproductive Technique

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Proposing quantum phenomena in neural events and cognition (Review)

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Introduction: More than a century ago, Max Planck proposed the quantization of energy to solve a problem called the ultraviolet catastrophe. Louis de Broglie also claimed that particles exhibit wave behavior. Davison-Germer tested Louis de Broglie's theory and obtained results that were consistent with the theory. Wave behavior occurs due to the smallness of Planck's constant in the scales of elementary, atomic, and molecular particles. The first person who tried to find a connection between the quantum and the brain was Alfred Lotka in 1925, and it was the beginning of entering the strange world of quantum mechanics and its role in neuroscience. The Orch-OR theory, developed by Roger Penrose and Stuart Hamroff in recent years, has helped draw attention to quantum mechanics' effects on the brain. There have been articles published regarding quantum phenomena that may occur at the synapse in recent years. The uncertainty phenomenon occurs when sodium and potassium ions pass through their channels. Due to the effect of quantum mechanics in the creation of spin chemistry, quantum mechanics can be indirectly considered as the cause of the development of neurochemistry. Quantum tunneling can also occur when neurotransmitters are released at the synapse. A photon is a quantum of energy in electromagnetic radiation and is known as a massless particle, so when examining the effects of light on the retina, the interaction should be considered quantum. The measurement problem is an unanswered question in quantum physics, theories related to the influence of the conscious observer on the collapse of wave function have been given, which may reveal a connection between consciousness and quantum mechanics. Brain function cannot be explained digitally with 0 and 1, so maybe we need quantum mechanics concepts for these things that happen at the moment, and we call them inspiration. Today, some researches in quantum biology about the mechanism of olfactory sense and magnetic orientation in birds, such as the European red-breasted bird (robin) are ongoing based on quantum mechanics.

Methods: A review of articles on quantum consciousness, quantum neuroscience, quantum brain, and quantum biology.

Results: Although people resisted the use of quantum mechanics in neuroscience in the last century, at least today they have understood that only using classical physics is not enough to explain neurocognitive phenomena.

Conclusion: While quantum phenomena occur at the microscopic level, humans are unable to observe them at the macroscopic level due to the low Planck's constant. Although several mental and cognitive activities of the nervous system are probably on this scale, perhaps by designing creative research projects using the latest new technologies presented in quantum physics, it is possible to decipher some mysterious cognitive mechanisms with quantum mechanics.

Keywords: quantum; consciousness; Neuroquantology; quantum brain

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Prostate cancer diagnosis with the aid of deep learning in multi-parametric magnetic resonance images (Review)

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Introduction: Prostate cancer is the second most common malignancy among men globally. Magnetic resonance imaging (MRI) is a useful method in prostate cancer detection. MRI has some benefits such as being a non-ionizing and highly sensitive approach. multiparametric MRI(mpMRI) protocols for prostate cancer detection Aim to increase sensitivity and specificity by compounding anatomical sequences of T1-weighted images (T1WI) and multiplanar T2-weighted images (T2WI) with functional sequences of diffusion-weighted imaging (DWI) and dynamic contrast enhancement (DCE)MRI. mpMRI is used to decrease needless biopsies. mpMRI shows high accuracy and specificity for recognizing clinically significant prostate can r. However, the diagnosis of prostate cancer via mpMRI highly depends on radiologists' expertise. In recent years, Deep learning has been designed for a wide range of applications in medical imaging. Therefore this review aims to investigate the abilities of deep learning methods in diagnosing prostate cancer using mpMRI.

Methods: This search was conducted in the Google Scholar database with the following keywords: “prostate cancer” in the title and” diagnosis” and “deep learning” and “magnetic resonance imaging” or “MRI” or “mpMRI” in all fields. We limited the publication time to after 2022 to evaluate the most recent literature. We also used the PubMed database for extra literature searches. In addition, relevant works published on the mentioned scientific websites were investigated. After screening the abstracts, we selected the relevant articles for this study.

Results: The total number of papers obtained through the search was 517. We limited our results to 39 papers based on the inclusion values. Among deep learning tactics, convolution neural network (CNN) is the most potent network which is skilled in extracting strong features from the input images that contemplate features from the low to the high level. there are other pre-

trained deep learning models such as MobileNetV2, ResNet50V2, Resnet101V2, Resnet152V2, Xception, InceptionResNetV2, and InceptionV3 which could be valuable to detect prostate cancer from given image groups. Many studies showed that mpMRI has a high sensitivity in detecting prostate cancer (more than 85%) also in many studies, it has been said that the diagnostic accuracy of detecting prostate lesions has increased with the help of deep learning.

Conclusion: Deep learning has the potential to improve diagnostic accuracy and reduce subjective decision-making in the process of cancer prediction. Deep learning has the "learn" ability, this ability is obtained through the analysis of features and complex image data and structures. The reviewed articles showed that the Deep learning techniques applied to mpMRI, seem to be an effective assistant in predicting and detecting prostate cancer lesions. This paper reports that the ability of deep learning to play a complementary role could aid radiologists in better diagnosis of prostate lesions.

Keywords: prostate cancer, magnetic resonance imaging, deep learning, diagnosis

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Protectivity of combination of outer membrane proteins Omp34 and BauA against Acinetobacter baumannii infection in murine model (Research Paper)

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Introduction: Acinetobacter baumannii is the most important agent of hospital-acquired infections worldwide. This bacterium has been regarded as a low-grade but an important opportunistic pathogen that causes various types of infections, including ventilator-associated pneumonia, urinary tract infection, skin and wound infections, bacteremia, and meningitis. Recombinant vaccines and specific antibodies are a new treatment strategies for such antibiotic-resistant infectious bacteria. However, a small number of bacterial surface antigens were tested that could only provide partial protection. For this reason, polyvalent (multiple) vaccines containing different antigens are needed to provide an acceptable level of protection. This study is oriented on the use of two outer membrane proteins, BauA and Omp34 as a polyvalent vaccine.

Methods: Recombinant BauA and Omp34 proteins were expressed, purified, and injected into BALB/c mice individually and in combination. Both active and passive immunizations were carried out. The mice were then challenged with a clinical isolate of A.baumannii. Then, the level of antibody in mice was measured by Indirect ELISA. The animal survival rate was also determined.

Results: Elevated antibody production was noted by ELISA in all the immunized groups. The combination of BauA and Omp34 proteins rendered good protection compared to the single administration of each protein

Conclusion: These data indicate that antibodies to protein antigens can boost immunity and protection against A. baumannii strains. The findings are supporting use of multivalent monoclonal antibody therapy to control infections caused by A. baumannii. We can therefore suggest the designed hybrid antigens as novel immunogenic candidates for developing effective subunit vaccine against A. baumannii infection

Keywords: Acinetobacter baumunnii ., Recombinant protein., BauA., Omp34., Vaccine

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Pseudomonas aeruginosa and the Biodegradation of Low-Density Polyethylene (LDPE) (Review)

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1.
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Introduction: Low-density polyethylene (LDPE) is one of the most widely used materials today. Unfortunately, LDPE has slow degradation after disposal, which lead to environmental pollution and endangering ecosystems. Therefore, we need effective methods to reduce LDPE pollution in our environment. Biodegradation by microorganisms is a green approach that can help address this issue. In this overview, we will present the roles of some Pseudomonas aeruginosa species in LDPE degradation.

Methods: As plastic usage has increased, the issue of post-consumer recycling has gained significant importance. Low-density polyethylene (LDPE) is a linear hydrocarbon polymer composed of long chains of ethylene monomers (C2H4) and constitutes a substantial portion of plastic waste. The degradation of low-density polyethylene (LDPE) in natural environments is a slow process which influenced by various environmental factors, including pH levels, atmospheric moisture, humidity, temperature, and exposure to solar radiation. The utilization of landfills may be viewed as a viable strategy; however, it comes with specific constraints. These constraints include an extended period required for decomposition and the discharge of harmful pollutants recognized to be linked to various human illnesses, notably cancer. therefore, microorganism biodegradation's ability gives us the chance to degrade plastic waste with fewer harms.

Results: Among the biodegradation methods, bacterial usage is one of the effective ways to control the problem. Pseudomonas aeruginosa is a Gram-negative bacterial species belonging to the Pseudomonadaceae family in the Gammaproteobacteria class, and it is one of the most commonly reported bacteria for this purpose. One of the reports about Pseudomonas aeruginosa includes the ISJ14 strain, which was isolated from a waste dump and demonstrated biodegradation ability at 37 °C without causing any danger to human health and the environment.[1] Pseudomonas aeruginosa E7 strain is another bacterium isolated from beach soil, which was previously contaminated by oil spills. The degradation system consists of alkane hydroxylase genes, such as rubredoxin reductase, rubredoxin, and alkane monooxygenase.[2] Another study reports on P. aeruginosa isolated from the

surface water of Yaounde, showing the ability to degrade materials under acidic pH conditions and at low temperatures (7°C and 23 ± 1°C) in the environment.[3] In the research conducted by Kyaw et al., they studied four bacterial strains, two of which belonged to the Pseudomonas aeruginosa species. They assessed the abilities of Pseudomonas aeruginosa (PAO1) and Pseudomonas aeruginosa (ATCC) strains using different methods. After a 120-day incubation period, weight loss measurements were recorded, with Pseudomonas aeruginosa (PAO1) strain demonstrating a 20% reduction in weight, while Pseudomonas aeruginosa (ATCC) strain showed an 11% reduction. They assessed the Mechanical Properties through extension at break (EAB) and initial tensile strength (TS) measurements after 120 days of incubation. For Pseudomonas aeruginosa PAO1, the EAB measurement showed a reduction to 79 mm ± 3%, while the TS reduced to -0.00078 ± 0.00011 MPa. In the case of Pseudomonas aeruginosa ATCC, the EAB measurement decreased to 92 mm ± 3%, and the TS reduced to 0.00026 ± 0.0002 MPa. They also assessed structural changes using Fourier Transform Infrared (FTIR). Pseudomonas aeruginosa PAO1 caused an 80% reduction, while Pseudomonas aeruginosa ATCC resulted in a 16% reduction.[4] Dwicania et al. conducted a study on a bacterial mixture consisting of Brevibacterium sp. and Pseudomonas aeruginosa and their impact on Linear Low-Density Polyethylene (LLDPE). The mixed culture was obtained from the Biology/Environmental Microbiology Laboratory at the Environmental Engineering Department of Trisakti University. They analyzed the effect of the mixture on LLDPE using Fourier Transform Infrared (FTIR), which revealed a reduction in intensity.[5]

Conclusion: Pseudomonas aeruginosa is one of the successful bacteria in LDPE biodegradation. Different study results have shown a reduction in the physical and biochemical LDPE samples. Although some genes and pathways that are involved in LDPE biodegradation are known today, we need more studies to understand the molecular mechanisms.

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Keywords: Low-density polyethylene (LDPE)-Biodegradation

Quick and Simple Methods to SNPs Identification (Review)

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Introduction: The most frequent source of genetic diversity across individuals is single-nucleotide polymorphisms (SNPs). The most frequent source of genetic diversity across individuals is single-nucleotide polymorphisms (SNPs). SNPs can currently be found using a variety of techniques. DNA sequencing is a common method for detecting SNPs, but it requires a laboratory environment for sample processing as well as bulky, expensive, and slow DNA sequencing equipment. Here, we describe some easier and faster methods for identifying SNPs. It is also recommended to select a cost-effective technique. ARMS or As-PCR: The Allele-Specific PCR technique was created for allele analysis of clinically important alterations. The introduction of intentional mismatches inside the three bases at the 3' end of the primers may help with accurate discriminating between two alleles. Two complementary reactions make up a typical ARMS test that can identify a known SNP polymorphism: one contains an ARMS primer specific for the wild DNA sequence and cannot amplify the mutated DNA at a particular locus, and the other contains a specific mutated primer and does not amplify wild DNA. As a result, this strategy is one of several used to identify SNPs. HRM-PCR: A quick and easy method for genotyping, mutation scanning, and sequence matching is high-resolution melting (HRM) of DNA. This technique, which helps to overcome conventional approaches and prepares for high performance, is based on measuring the fluorescence change connected to the melting temperature of double-stranded DNA in the presence of a dye mixed with saturated DNA, known as intercalating dyes, in real-time PCR reactions. Due to the specificity and sensitivity of the DNA melting curve profiles created by HRM analysis, different nucleic acid species can be identified based on minute sequence variations. PCR-RFLP: This technique involves treating a PCR amplicon with a particular restriction enzyme that causes the DNA to be cut at a distinct restriction site known as the recognition site, resulting in numerous DNA fragments of various sizes. The digested

amplicons are then placed on a gel and exposed to an electric field. Throughout the gel, bands of varying sizes move at varying intervals. The two main drawbacks of PCR-RFLP are the requirement for specialized RE and the challenge of accurately detecting changes when several SNPs are targeted at once. LAMP: loop-mediated isothermal amplification, is a quick and reliable technique for nucleic acid sequence-specific detection. The LAMP approach employs four sets of primers that are specifically designed to isolate six different areas of the target gene. The SNP-LAMP mismatch is caused by the SNP being at the 3' end of the LAMP primer, which results in the mismatch and hinders polymerase extension in the presence of a non-SNP sequence. This is how the LAMP method was established for SNP detection.

Methods: Articles required for the study were found using Google Scholar, PubMed, and MDPI searches.

Results: In this study, fast detection methods were investigated for identifying SNPs. ARMS-PCR, HRM-PCR, PCR-RFLP, and LAMP techniques were among those obtained in this study. According to research, ARMS-PCR is the most common and easiest approach for detecting SNPs. Specific primers are easily designed in this approach, after which PCR is done and the products are electrophoresed. In this technique, handling these processes and analyzing the results is easier and faster than in HRM-PCR, PCR-RFLP, and LAMP.

Conclusion: The analysis of the papers reveals that As-PCR is the most common, straightforward method for detecting SNPs. In many studies, this method has been developed to identify SNPs. Additionally, the comparison of various approaches demonstrates that, unlike other methods, it is more challenging to analyze HRM curves. Although AS-PCR involves more handling steps than HRM-PCR, it was the most time- and cost-efficient approach tested since it allows for straightforward and quick interpretation of the results and can be carried out using common laboratory equipment. PCR-RFLP techniques require more handling steps, have longer pause times, and cost more in materials. The LAMP method requires probes, which raises cost.

Keywords: SNP detection, As-PCR, ARMS-PCR, fast detection, simple method

Recent Advances in Application of Fucoidan in Wound Healing: A Systematic Review (Review)

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Introduction: Wound healing is a complex process that involves multiple cellular and molecular events. Fucoidan, a sulfated polysaccharide found in brown seaweed, has been shown to have anti-inflammatory, antioxidant, and immunomodulatory effects. The aim of this systematic review is to evaluate the potential of fucoidan as a therapeutic agent for wound healing.

Methods: A comprehensive search was conducted using PubMed from inception until May 2023. Studies that investigated the effects of fucoidan on wound healing in animal models or in vitro were included.

Results: A total of 51 studies were included in this review. All studies were conducted on animal models or in vitro and evaluated the effects of fucoidan on wound healing parameters such as wound closure rate, angiogenesis, collagen deposition, and inflammatory response. The results consistently demonstrated that fucoidan supplementation improved wound healing outcomes, including increased wound closure rate, enhanced angiogenesis, increased collagen deposition, and decreased inflammatory response.

Conclusion: Fucoidan has potential as a therapeutic agent for wound healing. The antiinflammatory, antioxidant, and immunomodulatory effects of fucoidan may contribute to its beneficial effects on wound healing outcomes.

Further studies are required to investigate the safety and efficacy of fucoidan in human subjects with various types of wounds. Fucoidan may represent a promising complementary therapy for wound healing

Keywords: fucoidan, wound healing

Recombinant Immunotherapeutic for cancer therapy: A Promising New Frontier (Review)

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Introduction: Nowadays, there is a growing curiosity about novel cancer treatments that influence on fate of millions of people worldwide. Immunotherapy is one of them. One bright area in immunotherapy is the development of recombinant immunotherapeutics. Recombinant immunotherapeutics are a class of drugs that are produced by integrating various proteins or heritable material from different sources to make a unique patch that can stimulate the immune system in distinguishing ways to eliminate cancer cells. These medicines, unlike traditional chemotherapy ones, specifically target cancerous cells by binding to their surface receptors and the other biomarkers particularly associated with tumorous cells. Immunotoxins, ADCs, and CAR T cells are exemplifications of them. However, several challenges need to be addressed, including the development of resistance and toxins associated with these curatives. We'll discuss some types of recombinant immunotherapeutics for cancer and their implicit benefits and challenges in the following sections.

Methods: This study has been performed by searching various texts, authoritative scientific articles, and several keywords such as cancer, protein therapeutics, recombinant proteins, and so on to find all relevant publications on recombinant immunotherapeutic -based approaches for cancer therapy. The articles used in this study are extracted from PubMed, Web of Science, Scopus and Google Scholar databases from 2017 to 2022.

Results: According to the findings, recombinant immunotherapeutics are designed to be specific to target cancer cells. Some of them include (A) Immunotoxins which are fusion proteins that are developed to widely attach to cancer cells specific antigen, offering a lethal dose of toxin directly to the cancer cell. Immunotoxins are helpful in clinical usage in cases of hematologic

malignancies. B) Antibody-drug conjugates (ADCs) are an antibody that targets a specific antigen on cancer cells, conjoined to a cytotoxic medicine. Once the ADC binds to the cancer cell, it discharges the cytotoxic medicine into the cancer cell, conducting to cell death. ADCs have shown usage in several types of cancer, including breast cancer and lymphoma. (C) Chimeric antigen receptor or (CAR) T cells are another recombinant immunotherapeutics that activate the immune system to eliminate cancerous cells. This therapy has been used in patients with hematologic malignancies like non-Hodgkin's lymphomaacute and lymphoblastic leukemia. (D) Checkpoint inhibitors, work by blocking checkpoint proteins from binding with their partner proteins. This prevents the “off” signal from being sent, allowing the T cells to kill cancer cells ;(E) Cytokines, which are proteins that stimulate the immune system; and (F) vaccines, which can stimulate the immune system to fight against cancer cells. Another important point to mention is the development of resistance, Toxicity and side effects associated with it. Immunotoxins and ADCs can drive off-target toxins due to the expression of the target antigen on normal cells. CAR T cells can lead to cytokine release and neurotoxicity, which can be life-treating.

Conclusion: Overall, recombinant immunotherapeutics represent promising tools in the treatment of cancer. These medicines have shown remarkable success in preclinical and clinical studies. Although numerous challenges need to be overcome it’s hoped that recombinant immunotherapeutics will become an important tool in the fight against cancer in the next years.

Keywords: Cancer, protein therapeutics, recombinant proteins, recombinant immunotherapeutic

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Recombinase-based amplification method as a promising tool for rapid molecular detection of Serratia marcescens (Research Paper)

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Introduction: Serratia marcescens is known to cause outbreaks in hospitals and is considered opportunistic. The World Health Organization stressed the need for new antibiotics to treat this bacterium in 2017 due to the bacterium's resistance to various antibiotics, which has made it challenging to treat. Rapid detection methods, such as isothermal nucleic acid techniques, have emerged as a reliable and fast way to identify bacteria. These methods can be performed at a consistent temperature and could aid in controlling the spread of S. marcescens and ultimately reduce its impact on public health. In this study, an isothermal amplification method was developed to detect S. marcescens.

Methods: To target a specific gene in the whole genome of S. marcescens, specific primers were designed. Nucleic acids from S. marcescens and eleven other related bacteria were extracted using the boiling method. The isothermal amplification technique was used to amplify the targeted gene, and hydroxy naphthol blue was added for colorimetric detection of the products. To ensure the accuracy of the study, DNA from eleven other related bacteria and S. marcescens was used. The sensitivity was evaluated using samples with different dilutions of DNA from S. marcescens.

Results: The isothermal method that was developed can detect the existence of S. marcescens DNA by amplifying the targeted gene within just 20 minutes at a temperature of 65°C. A positive sample containing S. marcescens DNA exhibited a clear sky-blue color change, whereas negative samples that contained DNA from eleven other bacteria changed to purple and dark blue. The specificity of the test was found to be 100% and the sensitivity was 94×10-3 ng/mL.

Conclusion: The initial report on the implementation of the developed isothermal method for detecting S. marcescens showed high speed, high sensitivity and precision to detect the bacterium at the point-of-care level. This

method has the potential for detecting and preventing S. marcescens outbreaks at an early stage.

Keywords: Serratia marcescens, isothermal amplification, colorimetric method, nosocomial infection

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Reduction of PCAT-29 long non-coding RNA in children with Autism Spectrum Disorder (Research Paper)

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Introduction: Autism spectrum disorder (ASD) is a common neurodevelopmental disorder in children, which refers to a heterogeneous group of impaired neurodevelopmental conditions. The prevalence of ASD has significantly increased over the past 20 years. ASD has a complicated etiology consisting of hundreds of genes and environmental factors. Mainly hereditary factors, history of psychiatric disorders of parents, fetal exposure to psychotropic drugs, and pre-term births are proposed as risk factors for this disorder. Long noncoding RNAs (lncRNAs) have been reported to affect neurodevelopment, thus participating in the risk of autism spectrum disorder (ASD). In the current work, we assessed the expression level of lncRNAs, PCAT-29, in the peripheral blood of children with ASD compared with healthy controls.

Methods: This study was performed using blood samples of 30 children with ASD and 41 healthy controls between the ages of 4 and 15 years old. Peripheral blood was collected from the two mentioned populations. RNA extraction and cDNA synthesis have been done on each blood sample. Specific forward and reverse primers were designed for PCAT-29 and quantitative Real-Time PCR was performed. Graph Pad Prism6 software was used for statistical analysis.

Results: Our study demonstrated that the expression level of PCAT-29 (P value= 0003) was significantly different between ASD patients and healthy control populations. In ASD cases, expression of PCAT-29 was reduced 60 times compared to healthy children. The results of pairwise correlation analysis between expression levels of PCAT-29 in ASD patients and control samples, there was no significant correlation of expression of PCAT-29 between these two populations. Using ROC Curve analysis, the specificity and sensitivity of the expression levels of PCAT-29 were evaluated. The results showed that PCAT-29 with an era under the curve (AUC) of 0.743 and

a P value of 0.0005 (sensitivity= 60%, specificity= 80.49%, and cut-off> 5.561) could be used as a diagnostic biomarker for ASD patients.

Conclusion: The result of this study provides clues for an association between the downregulation of PCAT-29 and ASD and also introduces PCAT-29 as a potential diagnostic biomarker for ASD. Generally, diagnosis of ASD is done by scanning social communications and interactions and other behavioral characteristics of patients. Due to the overlapping of some symptoms of ASD with other neurodevelopmental disorders, diagnosis of autism can be extremely complicated and time-consuming; so, using PCAT-29 or other long non-coding RNAs as diagnostic biomarkers for ASD, could be a fast and non-invasive method for diagnosis of named disorder. Due to some limitations that this study faced, further investigations are needed to prove and clarify the mechanism of the contribution of PCAT-29 in pathogen pathways in ASD.

Keywords: Autism spectrum disorder, PCAT-29, lncRNAs, diagnostic biomarker, real-time PCR

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Relation between sociodemographic factors and preterm birth
(Research Paper)

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Introduction: Preterm birth is a multi-risk factor. The leading causes of preterm birth are spontaneous, preterm premature rupture of the membranes, maternal and fetal inductions, and multiple pregnancies. Leading to preterm birth, factors such as socio-demographics can help health workers take necessary measures to mothers at risk in order to reduce maternal and fetal complications of premature birth.

Methods: The study was conducted on 5747 mothers who gave birth in 2016-2017. We used a researcher-made checklist based on scientific texts and articles to generate information on their pregnancies and births. The final checklist data was entered in SPSS software version 16. The logistic regression model was used to determine the socio-demographic factors associated with preterm birth.

Results: we realized that there are significant associations between socio-demographic factors during pregnancy and preterm birth. Maternal age younger than 18 , older than 35 years old, elementary education ,and illiterate have a significant association with preterm birth. The place of residence of mothers was not associated with the risk of preterm birth.

Conclusion: Maternal age and Mother's education level are associated with preterm birth. However, there is no relationship between the place of living of mothers and preterm birth.

Keywords: Preterm birth, sociodemographic, premature, risk factor

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Relationship between Phosphatase and Tensin Gene Expression and Clinicopathologic Features of Breast Cancer in Patients who Underwent Biopsy or Breast Surgery (Research Paper)

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Introduction: Phosphatase and tensin (PTEN) gene is a tumor suppressor gene on chromosome 10q23 that is composed of 11 exons. Several studies have shown that loss of PTEN function is a common occurrence in breast cancer in particular in triple negative type, and it is significantly associated with age and higher stage of cancer. In this study, the expression of this gene in malignant breast cancer tissue samples and their correlation with clinicopathologic parameters was studied.

Methods: In this retrospective study, 65 malignant tissue samples were chosen for immunohistochemistry (IHC) test. Other information about clinicopathologic features were collected from pathology reports and patients' medical records. IHC on the selected paraffin blocks was performed, and the collected data were analyzed using SPSS software and chi-square test. $P < 0.0500$ was considered statistically significant.

Results: PTEN expression rate in malignant breast tissue was 50.8% of the cases (33 out of 65 samples). Lack of PTEN expression had significant correlation with involvement of the lymph node sent by the sample, vascular or perineural invasion, metastasis and chemotherapy background, spontaneous malignancy presence, familial history, negative progesterone

receptor, negative estrogen receptor, and positive her2/neu. No relationship was observed between the expression of PTEN with patients' age, tumor size, age group of the patients after categorization into two groups of under 50 years and over 50 years, lesion location (left or right breast), and tumor grade.

Conclusion: The results showed PTEN loss as a frequent event in breast cancer that is closely associated with progression and poor prognosis. PTEN loss might predict more aggressive behavior and worse outcomes in patients with breast cancer.

Keywords: Phosphatase and tensin protein; Gene expression; Pathological fracture; Breast cancer

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Relationship between trigger point points and tinnitus in patients referred to the ENT ward of Ahvaz hospitals (Research Paper)

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Introduction: Trigger points are nodules in the muscles that surrounded by a rigid tissue. Therefore, this study performed to investigate the relationship between trigger points and tinnitus.

Methods: 60 participants with an age range of 18 to 55 years, including 30 women and 30 men with inclusion criteria that include persistent or intermittent tinnitus and complaints of pain (in the head, neck or shoulder girdle) during the past 3 months Presence of at least one active myofascial trigger points on physical examination, age 18-55 years, both sexes, with a sensitive tactile point in the upper trapezius muscle. Production of pain in the person when touching, the sign of a jump marked by the patient's voice or withdrawal, restriction of neck movements due to pain, was chosen.The severity of tinnitus was recorded by numerical rating scale (NRS), then the trigger points of pain were measured by algometer and the limitation of neck movement with a goniometer, and then the relationship between them and tinnitus was determined.

Results: The rate of tinnitus in the left ear was 53.3% and in the right ear was 46.7%. The mean score of tinnitus among patients was 5.38 with a standard deviation of 1.99. In this study, no significant relationship was found between trigger points and tinnitus.

Conclusion: The results showed that there is no relationship between trigger points and tinnitus according to the variables of age groups, type of sex, comorbid disease, level of education, ear side and tinnitus time.

Keywords: Tinnitus, trigger points, comorbidities

Relevance of fatty liver disease with daily habits (Review)

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Introduction: The term fatty liver covers a range of pathological changes. The basic entity comprising fatty liver is fat deposition within hepatocytes, also known as steatosis. Hepatic steatosis can be seen in many settings related to alcohol, chronic hepatitis C, and Wilson's disease. Many drugs can also produce hepatic steatosis; steroids, tamoxifen, and amiodarone are among the most frequent offenders. The commonest cause of steatosis is non-alcoholic fatty liver disease (NAFLD) not associated with any of the above situations, and the rest of this article will concentrate on this condition. NAFLD describes a spectrum of pathological changes in the liver ranging from fat alone (steatosis), through non-alcoholic steatohepatitis (NASH), to what has in the past been labeled as cryptogenic cirrhosis. NAFLD is recognized as being increasingly common in the Western world, concomitant with the risk factors for this condition – obesity, hyperlipidemia, and type II diabetes mellitus in particular. In the UK 4% of the population has abnormal liver function tests, of which around half are thought to relate to NAFLD. Data from autopsies in the USA suggest a prevalence of 6.3%, with the condition found in 7–11% of liver biopsies in North America, as compared to a much lower incidence in Japan (Reid, 2001). Incidence increases with age, and with the emerging epidemic of obesity, it is felt that the prevalence of NAFLD will significantly rise. Most commonly, NAFLD is asymptomatic. If symptoms are present, those most frequently described include lethargy and mild right upper quadrant discomfort. There are usually no specific abnormal signs on examination in NAFLD. The most frequently observed abnormal finding is hepatomegaly. Spider naevi has been described, and splenomegaly in up to 25% of cases. The presence of splenomegaly is unexplained, as it is not a sign of portal hypertension in the majority of these patients.

Methods: Three hundred and eight (mean age 21.72 ± 3.71 years) NAFLD patients were included in the study. After baseline anthropometric measurement i.e., body mass index (BMI), and waist circumference (WC); we assessed markers of NAFLD including an ultrasound scan (USS) determined fatty liver. Healthy and Western dietary patterns were identified using factor analysis and all participants received a z-score for these patterns. Prospective

associations between the dietary pattern scores and risk of NAFLD were analyzed using multiple logistic regression.

Results: NAFLD was present in 21.7 % of adolescents. A higher BMI, a higher Waist, a lower daily hours of sleep, a lower No. of meals/day, a lower AMDA, a higher grams of alcohol, a higher No. of cigarettes, smoking/per day, and a lower Cup of coffee/per day were associated with a greater risk of NAFLD in adolescents. However, healthy daily habits in adolescents appeared protective against NAFLD, whereas unhealthy daily habits were associated with an increased risk of NAFLD.

Conclusion: Daily habits of adolescents in a general population sample were associated with an increased risk of NAFLD, particularly in obese adolescents. In this study, we assessed liver health using USS to determine the presence of fat in the liver. There were no known cases of liver disease in this cross-sectional study and we didn't remove the number of participants who had reported consistent harmful drinking. Therefore, it is reasonable to assume that in our cross-sectional, USS-determined fatty liver is likely to represent NAFLD. The aim of our study was firstly to examine the associations of NAFLD with daily habits and secondly to consider whether these associations are confounded by daily habits. The results demonstrate that for USS determined NAFLD there were positive associations with daily habits.

Keywords: NAFLD, Daily habits, Adolescents

Reparative effects of local and intraperitoneal application of platelet-rich plasma (PRP) in hypothalamic arcuate nucleus lesion model in female rats. (Research Paper)

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Introduction: In female rats, chemical destruction of the arcuate nucleus causes the cessation of sexual cycles (estrous cycle). In this regard, if the arcuate nucleus is reconstructed and repaired, it is possible to re-establish the estrus cycles. In this research, the restorative or protective effects of PRP on the neurons of the arcuate nucleus were investigated in several different time periods after the destruction of the arcuate nucleus.

Methods: 90 female Wistar rats were divided into 8 experimental groups (n=10) and a control group. The experimental groups included the negative control (bilateral destruction of the arcuate nucleus with quinolinic acid) and the groups receiving local PRP included immediately, 24h, 48h, 72h, (immediately and 24h), (immediately and 24h and 48h), (immediately and 24h and 48h and (They were divided 72h after creating a bilateral lesion in the arcuate nucleus. Then, after 2.5 months of daily smearing, the mice were deeply anesthetized and the brain was removed for RT PCR and brain and ovary for histological studies.

Results: Creating a bilateral lesion of the arcuate nucleus with quinolinic acid causes the cessation or disruption of the estrus cycle, and the administration of PRP protects or restores the arcuate nucleus. The time of post-injury administration and the number of administrations are important in the effects of PRP, and the earlier the application of PRP, the more evident its reparative effects. Counting the neuronal density in the arcuate nucleus and ovarian weight and counting the primary ovarian follicles in the groups receiving local PRP showed a significant difference from each other ($P<0.001$)), a significant decrease compared to the healthy control group ($P<0.01$) and a significant increase with the negative control group ($p<0.01$). The relative mRNA expression of case peptin, neurokinin B and dynorphin in the groups receiving

local PRP is significantly different from each other (P<0.001), a significant decrease compared to the healthy control group (P<0.01) and a significant increase compared to the negative control group (p< 0.01).

Conclusion: The arcuate nucleus was used as a model to evaluate the ability of PRP in repairing nerve lesions or preventing the exacerbation of nerve lesions. Cessation of the estrous cycle and its resumption was considered as a measure to evaluate the restorative or protective effects of PRP. In this regard, the effects of the time factor after applying the lesion in the application of PRP as well as the number of times of its application were considered.

Keywords: Arcuate nucleus, Estrous cycle, Quinolinic Acide, PRP, KISS1, Neurokinin B, Dynorphine

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Revealing HSA Binding of Berberine Nanoparticles: An Empirical Exploration via Biophysical Approaches (Research Paper)

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Introduction: Berberine (BBR), an isoquinoline alkaloid from Berberis aristata, holds a rich history in traditional medicine and is the subject of modern scientific exploration. BBR has been integral to Ayurveda and traditional Chinese medicine, addressing ailments from hypertension to inflammation. It significantly lowers lipid levels by enhancing LDL receptor expression and has undergone clinical trials for anti-hyperlipidemic effects (3-5). BBR also inhibits cell invasion, metastasis, and influences cell proliferation, demonstrating anti-inflammatory and antioxidant properties (6-8). However, its potential is constrained by poor water solubility, first-pass metabolism, and limited absorption, necessitating high doses with potential side effects (3, 4, 9-11). Therefore, a particular nano-formulation method (the hydrothermal method) has been utilized in an attempt to overcome the issue of low water solubility and increase its potential therapeutic efficacy. HSA, the predominant protein in blood plasma, is a single-chain, none-glycosylated peptide exhibiting a helical structure comprised of extended loops and turns (with concentrations of 35–50 g/L in human serum and a molecular weight of 66.5 kDa). HSA has a high affinity for a wide range of molecules including exogeneous drugs and this affinity ultimately affects the distribution and bioavailability of drugs. Thus, this study was conducted to explore the intricate details and subtle aspects of the interaction between berberine nanoparticles (nBBR) and HSA, which can further be useful in designing drug delivery systems based on plasma proteins.

Methods: The nBBR was produced through the hydrothermal method, and the obtained particles were characterized using transmission electron microscopy (TEM) and dynamic light scattering (DLS). Moreover, the formation of the nBBR-HSA complex has been investigated using biophysical methods such as fluorescence spectroscopy, isothermal titration calorimetry, and circular dichroism (CD).

Results: The hydrodynamic radius (RH) and the size distribution of the synthesized nanoparticles were measured using the dynamic light scattering. Additionally, TEM micrographs were employed to analyze the morphology of the obtained nanoparticles (Fig. 1). Furthermore, fluorescence data of HSA revealed a strong emission with a maximum peak at 340 nm, which significantly reduced in a concentration-dependent manner in the presence of nBBR (Fig. 2). The experiment was conducted at different temperatures (298, 303, and 308 K), and the data were analyzed using the Stern-Volmer equation. The KSV values (on the order of 10^5 M^(-1)) exhibited a decrease as the temperature increased. To provide a quantitative description of the energetics of the interaction, thermodynamic measurements were performed using the van't Hoff method and ITC technique. According to the data, the formation of the nBBR-complex is associated with a positive entropy change (11.95 J.〖mol〗^(-1) K^(-1)) followed by a negative enthalpy change (-23.56 kJ.〖mol〗^(-1)). This results in a negative net ΔG^0 for the system. Moreover, negative (downward) peaks appeared in the ITC thermogram. The CD spectrum of HSA (Fig. 3) demonstrated the double minima at 208 and 222 nm, which are the characteristic of α-helical structure. Notably, the negative ellipticity increased upon the addition of nBBR, and the formation of the complex was accompanied by an enhancement in the α-helix and β sheets content percentage, along with a reduction in random coil structures.

Conclusion: In this empirical study, we synthesized berberine nanoparticles (nBBR) using the hydrothermal method and conducted a comprehensive analysis of their interaction with human serum albumin (HSA) through various biophysical techniques. Our analysis, as revealed by dynamic light scattering (DLS) and transmission electron microscopy (TEM) imaging, demonstrated that the produced particles exhibited an average size ranging from 50 to 70 nm, with a narrow size distribution and spherical morphology, aligning precisely with our anticipated outcomes. Furthermore, fluorescence data combined with Stern-Volmer analysis unequivocally confirmed the ability of nBBR to interact with HSA, forming a ground-state complex and eliciting structural alterations in the protein. Thermodynamic profile of the interaction underscored that the formation of nBBR-HSA complex is an energetically favorable, exothermic, and spontaneous process that regulates through electrostatic forces. Notably, the circular dichroism results unveiled the significant influence of nBBR in inducing conformational changes and promoting the development of a more ordered secondary structure in HSA, thereby enhancing its biological functionality. These findings collectively shed light on the binding behavior of nBBR-HSA complex, providing information that holds substantial implications in designing drug delivery systems

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Keywords: Berberine-HSA-Nanotechnology-Circular Dichroism, ITC

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Review of a new hemophilia treatment method (Review)

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Introduction: Hemophilia is an inheritance bleeding disorder that classified into different types based on mutations in the genes encoding coagulation factors. The inheritability of A and B types is recessive X-linked but the deficiency or dysfunction of coagulation factor VIII is related to the A and deficiency or absence of coagulation factor IX caused the B type. In comparison hemophilia B is often considered less severe than hemophilia A. Hemophilia A is the most common type. The rare one is the Hemophilia C that is due to the lack of factor XI, and the other rare kind is parahemophilia, caused by the lack of factor V. These can diagnose by determining the levels of the coagulation factors and the presentation levels of inhibitor factors. Three subtypes are available for the hemophilia A and B based on diagnostic levels of FVIII and IX activity is made severe, moderate and mild classes for each one exclusively. Since the hemophilia A is more common, in this review is tried to understand the basis of this disorder and discuss the novel methods of curing it. Nowadays the diagnosis and treatments are done by the molecular biology techniques.

Methods: This information is gathered by searching in the google scholar, one of the most popular research engines, in purpose for finding novel and up to date treatments in hemophilia since 2019. These searches were based on different types of hemophilia and hemophilia treatment in case of "molecular revolution", Bispecific "antibodies, "emicizumab therapy".

Results: As usual, human being always wants to find the best ways for curing diseases, so it's obvious that we have different methods in hemophilia treatment. The oldest using method was substitutive treatment by intravenous administration of factor VIII (FVIII) concentrates. Nowadays so many techniques have applied, the important point is that any method has its own advantages and disadvantages. And it needs to be suitable for the specific condition in each patient, because they could have had the other disorders beside hemophila in their body. So, recently, a lot of advances have expanded the therapeutic options for people with hemophilia, such as nonfactor therapies (emicizumab, fitusiran, and anti-tissue factor pathway inhibitor antibodies), extended half-life (EHL) products, gene therapy, RNA interference, even stem cell usage.

Conclusion: Disruptive molecular therapies have diversified the hemophilia therapy completely. The classic treatments have issues in efficacy, cost, availability, and side effects including the development of neutralizing antibodies. One of the nonfactor therapies, emicizumab, the first and only approved and increasingly accessible treatment option for hemophilia A, is a bispecific antibody that its structure is manufactured through genetic recombination, chemical conjugation or quadromas. Emicizumab mimics the action of factor VIII (FVIII) and it binds to both FIXa and FX inducing FXa generation in the early (extrinsic) stages. The most effective time of this bispecific antibody is for prophylaxis especially early in life due to avoid joints' damage that may cause repeated hemarthrosis. One usage of Bypassing agents is helping to restore haemostasis in inhibitor patients. In case of prophylaxis, emicizumab is administered subcutaneously once a week, reduced the number of bleeding episodes in patients with inhibitors significantly. The emicizumab does not need to be activated by thrombin so, intrinsic pathway-based laboratory tests, including activated clotting time and activated partial thromboplastin time, clotting times with emicizumab and so on used for measuring the efficiency of it. The latency persistence of emicizumab depends on different situations in patients and their physical activity, it has to be under consideration by different kinds of tests. In severe cases of hemophilia A, the combination of high-dose FVIII therapy, the classic method, and bypassing agents like emicizumab needs to employed. The problem of using this method back to inadequacy and lack of scope for required tests equipment in the world and needs to be more accessible for patients. This method requires a basis knowledge to be taught to patients and make them aware. These kinds of treatments, bispecific antibodies are going to be developed in the future and become more available that can make an enormous effect in many disorders.

Keywords: Hemophilia, Bispecific antibodies, Emicizumab , novel treatments.

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Review of Azoospermia: From Diagnosis to Treatment (Review)

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Introduction: The most severe form of male infertility is termed azoospermia, where no sperm are identified in semen. Azoospermia can be observed in about 1% of men. In terms of numbers, it is estimated to affect between 10% and 15% of men in infertile couples. Azoospermia is usually a condition with no noticeable symptoms. Affected men usually have no complaints.WHO recommends that two semen analyses be performed two to three months a part. If in the first and second semen analysis the sperm count is zero, the diagnosis of azoospermia is confirmed.

Methods: we were conducted used the PubMed/MEDLINE , EMBASE databases and search restrictions included the English.

Results: Azoospermia can be further divided into obstructive azoospermia (OA), as a result of an obstruction in the ejaculatory pathway or non-obstructive azoospermia (NOA), as a result of defective spermatogenesis .The reproductive prognosis in obstructive azoospermia is good. The Y chromosome is one of the smallest chromosomes in the human genome and only chromosome that can be missing entirely without lethal consequences . The Y chromosome is essential for testis development and spermatogenesis. The Y chromosome is generally divided into two domains, the pseudoautosomal regions (PAR1 and PAR2) and an area known as male specific Y region (MSY). Within the MSY and on the long arm of the Y chromosome, are regions known as the azoospermia factor (AZF) regions, which contain genes critical for spermatogenesis and male fertility .The AZFa region is the shortest of the regions, This region is found deleted about 0.5–4% of the time when AZF deletions are found . Despite being the smallest of the AZF regions, complete deletion leads to the most severe phenotype, Sertoli cell only Syndrome. The AZFb region is in the mid portion of Yq11 and overlapping with the AZFc region. It is generally accepted that AZFb deletions lead to azoospermia. AZFc is the largest of the coding regions and most complex. complete deletions are found in 80% of all AZF deletions . but AZFc have a 50% chance of retrieving sperm in testicular extraction.

Conclusion: most common genetic disorder causing NOA is the Klinefelter syndrome (KS), which is characterized by the presence of an extra X chromosome. However, there are other implications for beyond just the AZF deletions that can affect spermatogenesis. Copy number variations of DAZ, RBMY1, CDY1, TSPY1 the DYZ1 array, have all be implicated in affecting spermatogenesis. If the azoospermia is caused by a stress problem or a current drug, it sometimes helps to stop the causative agent. reduce the stress or stop taking the drug. If the root cause is a hormonal problem, as in hypogonadotropic hypogonadism, treatment with FSH may be effective in getting the testicles to produce sperm again. However, in obstructive azoospermia, the first treatment is surgical repair to remove the blockage and connect the ducts, and the second treatment, if surgical repair is not possible, is sperm extraction from the testis (TESE) or epididymis (PESA).

Keywords: Azoospermia, Male Infertility, Y Chromosome, Sertoli cell only, Testis

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Reviewing the methods of green synthesis of two nanoparticles applied in medical science; Gold and silver nanoparticles (Review)

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Introduction: According to the National Nanotechnology Initiative (NNI) definition, nanoparticles are structures with sizes from 1-100 nm in at least one dimension. There are different types of nanoparticles and each one has an exclusive set of properties and applications and can be synthesized by conventional or unconventional methods. Synthesis of nanoparticles can be done physically, chemically and green. Green synthesis produces stable nanoparticles that are environmentally friendly and economically viable. The growing popularity of green methods has led to the synthesis of nanoparticles using different sources such as plants, algae, microorganisms (bacteria, fungi, etc.), which has led to production on a larger scale with less pollution for the environment and human health. Silver and gold nanoparticles are considered noble metal nanoparticles (i.e. metals resistant to corrosion and oxidation). These metal nanoparticles have characteristics such as: high electrical and thermal conductivity, chemical stability, antimicrobial activity against a wide range of microorganisms. . In the green synthesis of nanoparticles, including gold and silver, unlike microorganisms, plants are completely used, that is, nanoparticles can be synthesized by using leaves, stems, flowers, seeds, roots, fruits, skins and latex of plants. Microorganisms such as fungi, bacteria, yeasts are of great interest for the synthesis of nanoparticles, but this process is threatened by culture contamination, long methods and less control over the size of nanoparticles. Gold and silver nanoparticles synthesized in a green way have a wide range of properties, including antibacterial, antifungal, antiviral, etc., and are widely used in the field of biomedicine, including cancer diagnosis and treatment, drug delivery, nanosensors, and biomarkers. Due to the great importance of green synthesis, in this article we have reviewed the recent methods of green synthesis of gold and silver nanoparticles.

Methods: Google scholar database was used to prepare this review article. 29 limited articles from 2019 to 2023 have been used with the aim of investigating the green synthesis of gold and silver nanoparticles and their biological applications. The key phrases used are respectively green synthesis of silver/gold nanoparticles by

Results: Each of the gold and silver nanoparticles synthesized by biological methods have a specific size and shape. The morphology (size and shape) of nanoparticles is determined by the reaction conditions so that they may have different shapes such as triangular, spherical, hexagonal, polyhedral, etc. Synthesized nanoparticles are analyzed using various techniques including UV-vis spectroscopy, FTIR, XRD, TEM, EDX, AFM, SPR, X-ray diffraction, etc. to confirm their characteristics as a nanoparticle. We arranged the information related to the comparison of gold and silver nanoparticle synthesis methods as well as the use of each in separate tables.

Conclusion: Green synthesis of gold and silver nanoparticles by bacteria or using natural extracts as biologically prepared reagents shows high solubility, performance and stability in the synthesized nanoparticles. The use of organisms or reagents of biological origin is considered one of the most promising methods because its cost is low, diverse natural resources are used, and it also helps to reduce the potential toxicity of nanoparticles. Metal nanoparticles such as gold are widely used as nanomaterials in cancer treatment, biomolecular screening, selective destruction of certain cells, etc., as well as silver nanoparticles with wide applications in drug delivery, nanomedicine, cosmetics, food industry and agriculture. It is suggested that in the future the green synthesis of these two nanoparticles will be done using other natural and biological materials and the characteristics of the methods will be compared.

Keywords: Green synthesis, gold nanoparticles, silver nanoparticles, microorganisms, plants

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RGD Immobilization on Carboxyl Surface-functionalized Electrospun Poly-ε-caprolactone Scaffolds Promotes Endothelialization and Anti-thrombotic Activity in a Perfusion Bioreactor (Research Paper)

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Introduction: Rapid endothelialization, endothelial cell stability, and prevention of thrombus formation by nitric oxide (NO) production, at the lumen of vascular electrospun poly-ε-caprolactone (PCL) scaffolds under blood flow is still a challenge. Surface-functionalization of PCL scaffolds with negatively-charged carboxyl (COOH) or positively-charged amine (NH2) groups, followed by immobilization of arginine-glycine-aspartate (RGD) onto the scaffold surface affects endothelialization and cell stability. However, whether RGD immobilization on COOH surface-functionalized electrospun PCL scaffolds is more effective than on NH2 surface-functionalized scaffolds under blood flow is unknown. In this study we aimed to test whether RGD immobilization on COOH or NH2 surface-functionalized electrospun PCL scaffolds affects endothelialization, endothelial cell stability, and NO production in a perfusion bioreactor mimicking blood flow.

Methods: Electrospinning: Hollow tubular PCL scaffolds (ø: 4 mm, length: 30 mm, thickness: 0.26 mm) were electrospun (30 kV; feed rate: 1.5 ml/h; distance: 15 cm) using 13% (wt/wt) PCL in ¼ (v/v) acetic acid/formic acid.

Surface functionalization and RGD immobilization: PCL scaffolds were surface-functionalized by carboxyl (PCL/COOH) or amine (PCL-NH2) functional groups using wet-chemical treatment with 3 M NaOH or 10% (wt/v) 1,6-hexamethydiamine (HMDA). RGD was immobilized on carboxyl (PCL-COOH/RGD) or amine (PCL/NH2/RGD)-functionalized PCL scaffolds. Scaffold characterization: The physicochemical properties of electrospun scaffolds, i.e. fiber diameter and distribution as well as pore size and distribution (ImageJ software), porosity (liquid-displacement assay), topography (scanning electron microscopy (SEM)), and hydrophilicity (water contact-angle) were determined. Cell culture and scaffold bioactivity: Human umbilical vein endothelial cells (HUVECs) were seeded at 105 cells/cm2 at the lumen of the scaffolds, and cultured in a static or perfusion bioreactor for 8 days. HUVECs proliferation (AlamarBlue® assay), collagen production (picrosirius red staining), NO production (Griess assay), and stability (AlamarBlue® fluorescent-assay) were assessed.

Results: COOH and NH2 surface-functionalization followed by RGD immobilization (PCL-COOH/RGD and PCL-NH2/RGD) decreased fiber diameter (0.4-0.5-fold) and water contact angle (0.3-0.7-fold), but increased pore size (1.7-2.1-fold) and porosity (1.2-fold). PCL-COOH/RGD and PCL-NH2/RGD increased cell proliferation (2.2-5.6-fold) and collagen deposition (1.4-1.7-fold) in a perfusion bioreactor after 8 days. PCL-COOH/RGD and PCL-NH2/RGD increased cellular NO production (1.2-4.2-fold) after 30 min in a perfusion bioreactor. PCL-COOH/RGD and PCL-NH2/RGD increased cell stability by decreasing cell detachment (PCL-COOH/RGD: 0.07-fold; PCL-NH2/RGD: 0.2-fold) after 1 h in a perfusion bioreactor. Cells were more stable on COOH surface-functionalized RGD immobilized (PCL-COOH/RGD) scaffolds compared to NH2 surface-functionalized RGD immobilized (PCL-NH2/RGD) scaffolds after 1 h in a perfusion bioreactor.

Conclusion: Maximum endothelialization, cell stability, and NO production were observed on carboxyl surface-functionalized electrospun PCL scaffolds followed by RGD immobilization, which might be promosing for long-term application of endothelial cells to prevent thrombus formation at the lumen of vascular scaffolds under blood flow.

Keywords: Amine functional group; Carboxyl functional group; Endothelialization; Perfusion bioreactor; RGD

RNA expression profils of HER2-possetive advanced gastric or gastroesophageal junction cancer and healthy gastric mucosa control FFPE samples (Research Paper)

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Introduction: Stomach (gastric) cancer is cancer that starts in the cells lining the stomach. The stomach is an organ on the left side of the upper abdomen that digests food. The stomach is part of the digestive tract, a series of hollow, muscular organs joined in a long, twisting tube from the mouth to the anus. Competitive endogenous RNAs (ce RNAs) theory have revealed a new mechanism of interaction between RNAs (mRNA-mi RNAs and lnc RNAs) that is used to find the involved genes.
In this study we used bioinformatics analysis and signaling pathway to target appropriate gene.

Methods: to begin with GSE220917 has been chosen from GEO to analysed genes with significant decrease/increase in expression regulation . ATP4A was selected and by using encore and Gepia2 checked the expression – survival and correlation analysis then used KEEG and Reactome and finally mRNA can establish a ceRNA network with miRwalk and miRNA was searched in LncRNAs 3.0. for pro-pro interacton used string and for miRNA-mRNA interaction used miwalk and for lncRNA-miRNA interaction used lncbase .

Results: after carefule analysis of a significant gene that effective on advanced gastric cancer (GSE220917) , a total number of 2000 differentially expressed genes (DEGs)were detected . ATP4A is a decreasing gene. DEGs with adjustedp –valu <0.05 and |logFC|>2 were considered significant. In encori and GEPIA2 analysed the expression and survival and we have significant p – valu and the correlations between ATP4A (decreaseasing gene) and UBD (increasing gene) were negative. And in keg and reactome this gene have impact on mineral obsorption and gastric acid secretion and Metallothioneins Bind Metals R-HSA – 5661231and many other pathways . After that in miRNASNP we found some SNP that the probable cause to decresead this gene. And we had negative deltaG duplex.Also p220648 was a protein that changed the Amino Acide in HOPE. Fainally ATP4A demonstrated a connection with has-miR-4787-5p in miR-walk. The picked mRNA was searched in LncBase.v.3. to make sure that the LncRNAs are correct we checked in a GeneCards .

Conclusion: The GSE220917 microarray dataset was used to identify difrentally expressed genes between GKN1 -GIF -PGC -ATP4A .
we select this significant gene and did a variation and use some sites to check a gene survival and the rate of deaths . We choose a ATP4A that have low express and check which SNP is on it and can be effective for low express so we approached top-down .We checked the interaction and this gene have a role in STAD cancer progression .

Keywords: systems biology , RNA interaction , High-throughput data analyss , pathway enrichment

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RNA-seq Analysis and Identification of Potential ceRNA Axes in Prostate Cancer Progression using Systems Biology Methods (Research Paper)

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Introduction: Prostate cancer is among the most common cancers in males. Recent application of system biology methods has resulted in identification of key genes in the process of carcinogenesis.

Methods: In the current study, we applied the system biology methods for identification of potential competing endogenous RNA axes in prostate cancer.

Results: Our analyses revealed importance of ADAMTS9-AS2/miR-150/PRKCA, ADAMTS9-AS2/miR-150/MMP14, MEG3/miR-150/PRKCA and MEG3/miR-150/MMP14. Remarkably, all hub genes within the key axes of the ceRNA network, except MEG3, exhibited strong statistical significance in survival analyses. Therefore, these genes can be regarded as prognostic markers in prostate cancer and potential candidates for therapeutic interventions.

Conclusion: Future studies can focus on transcriptional profiles of prostate cancer samples with different clinical stages to better understand stage-specific events.

Keywords: Prostate cancer, ceRNA, Key Axes, lncRNA

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Role of Cilia in Cancer (Review)

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Introduction: Besides the sensory role of the primary cilium in olfaction, the perception of light, and mechano-and chemo perception, it is increasingly being considered to be extremely important for cancer fate. Although tumors initiate from oncogenic changes in a cancer cell, subsequent tumor progression and therapeutic response depend on interactions between the cancer cells and the tumor microenvironment (TME). The primary cilium provides a spatially localized platform for signaling by Hedgehog, Notch, WNT and some receptor tyrosine kinase pathways and mechanosensation. Changes in ciliation of cancer cells and/or cells of the TME during tumor development enforce asymmetric intercellular signaling in the TME. Growing evidence indicates that some oncogenic signaling pathways as well as some targeted anticancer therapies induce ciliation, while others repress it.

Methods: Several tumor cell lines that become drug-resistant after chronic drug exposure showed a percentage increase in ciliogenesis and/or cilia length, with the appearance of cilia fragmentation. Finally, targeting ciliogenesis with a siRNA approach or the pharmacological inhibition of the Hedgehog pathway sensitized tumor cells to drugs and enhanced apoptosis.

Results: The links between the genomic profile of cancer cells, drug treatment and ciliary signalling in the TME likely affect tumour growth and therapeutic response. as well as clinical reports demonstrated an important role for cilia and cilia length in acquired, which are clinically relevant therapeutic agents primary cilia are interesting targets for novel therapeutic approaches. So-called “ciliotherapy” could be proposed, based on drug repurposing, which would enable the restoration of primary cilia in cilia-lacking cancer cells.

Conclusion: Primary cilia are interesting targets for novel therapeutic approaches. So-called “ciliotherapy” could be proposed, based on drug repurposing, which would enable the restoration of primary cilia in cilia-lacking cancer cells.

Keywords: ciliotherapy, Primary , siRNA, primary cilia

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Role of exosomes derived leukemic cells in leukemogeneis (Review)

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Introduction: Hematologic malignancies are a group of diseases with variable pathogenesis and prognosis, including lymphoid, myeloid, histiocytic, and mast cell neoplasms. The prognosis of these diseases depends mainly on the pathological nature of the cancer. Leukemias are a group of blood cancers called lymphocytic and myeloid leukemias, which are divided into two types, acute and chronic, depending on the origin of cell types and clinical symptoms. Current diagnostic tests for leukemia include flowcytometry, biopsy, and imaging studies. Age and gender as well as the type and speed of leukemia are important indicators in the treatment of patients. All living cells release extracellular vesicles (EVs), which are composed of lipid bilayer membranes. Extracellular vesicles include several types, including exosomes, micro vesicles (MVs), ectosomes, oncosomes, and apoptotic bodies. It is known that extracellular vesicles are a general name for secreted vesicles. Extracellular vesicles are not just a simple two-layer lipid membrane structure; They are important transporters of various bioactive molecules, and these components of extracellular vesicles can reflect the properties of the cells of origin. Extracellular vesicles circulate in extracellular spaces in biological fluids such as blood, ascites, urine and saliva. An important historical step in this research area has been the discovery of new functions of extracellular vesicles as mediators of cell-cell interactions, where extracellular vesicles can deliver functional molecules to recipient cells, leading to changes in their physiological and pathological functions. Intercellular communication is an essential process not only in pathological situations but also for normal homeostasis. This communication occurs through direct contact between cells or through secretory factors such as growth factors, cytokines and chemokines. In general, extracellular vesicles cover a wide range of vesicles ranging in size from 8 nm to several micrometers. The diameter of micro vesicles generally varies between 200 nm and several micrometers. This is despite the fact that exosomes are smaller, measuring between 50 and 100 nm in diameter. In this review, we focused on leukemia cell-derived exosomes in tumor progression.

Methods: This study is a review study that was conducted with English keywords, exosomes, micro vesicles, leukemic cells, cancer progression in reliable scientific databases such as PubMed, Google scholar in the period

from 2015 to 2023 and in the initial search 26 articles were found, and after evaluating the title and abstract, 8 articles were selected with the necessary conditions to participate in the present study, and general conclusions were made based on the information in the selected articles.

Results: Leukemia-derived exosomes can activate bone marrow stromal cells to improve leukemia cell survival, cell proliferation, and chemotherapy resistance. These exosomes disrupt the host's immune system, creating an immunosuppressive state and facilitating immune evasion of leukemia cells. They also transport proangiogenic molecules to endothelial cells, promoting angiogenesis and providing a favorable microenvironment for leukemia cells. A thorough understanding of the properties, biogenesis, and function of leukemia cell-derived exosomes, as well as the in vivo effects of exosomes on various components of the host immune system, could improve our ability to use exosomes as biomarkers and therapeutic targets.

Conclusion: leukemia cell-derived exosomes can play an important role in the life of leukemia cells and influence vital processes such as survival, proliferation and apoptosis of these cells. These exosomes contain biological molecules such as miRNA, proteins, mRNA, etc. that can shed light on the pathological condition of leukemia patients. These partially oncogenic biomolecules can be transferred to nearby or distant cells and affect the behavior of these recipient cells. Therefore, cellular communication via exosomes could play a potentially important role in the development of leukemia. It seems that the identification of prognostic values and their application to detect micro vesicles in leukemia could offer new therapeutic targets for monitoring the condition of leukemia patients.

Keywords: exosomes, micro vesicles, leukemic cells, cancer progression

Role of mesenchymal stem cells in the treatment of inflammatory bowel disease (Review)

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Introduction: Inflammatory bowel disease (IBD) is an autoimmune disease that are characterized by chronic inflammation of the gastrointestinal tract. This disease exists in two forms: ulcerative colitis and Crohn's disease. Both forms of the disease have increased the incidence of gastrointestinal malignancies and have led to a significant rise in morbidity and mortality due to this disease. Today, immunosuppressive drugs are used to treat inflammatory bowel disease, but due to the side effects of these drugs, satisfactory results are not achieved in many cases.

Methods: One of the best treatments for inflammatory bowel disease is treatment with stem cells, which simultaneously restores the damaged intestinal tissue on the one hand and improves immune system disorders on the other hand. Stem cells are cells that retain the ability to divide for a long time and differentiate into different types of specialized cells under appropriate conditions and signals. The mechanism of action of stem cells is twofold: one is the differentiation of mesenchymal stem cells into intestinal cells, which causes the replacement of lost cells. The other, through the secretion of immune system regulatory factors that control the activity of the body's immune system cells. These cells produce large amounts of cytokines that led to stimulate neutrophils chemotaxis and release of pro-inflammatory chemicals. Mesenchymal stem cells also increase the level of cytokine-10 and reduce the clinical symptoms of colon inflammation.

Results: In laboratory research, bone marrow mesenchymal cells were transformed into endothelial progenitor cells, and then differentiated into intestinal epithelial cells. These cells caused the construction of the basement membrane and the production of extracellular matrix. Other laboratory studies also showed the important role of these cells in the secretion of immune system regulatory factors that are specific to the intestinal tissue.

Conclusion: It is possible to obtain bone marrow stem cells autologously (taking stem cells from the patient's own bone marrow), and allogeneic (taking stem cells from the bone marrow of a donor), and both methods can be used to treat inflammatory bowel disease. The use of stem cells promises more

effective and efficient treatments for the treatment of inflammatory bowel disease. With the help of this method, the intestinal lost cells are replaced, intestinal inflammation is reduced, and there will be no side effects caused by immunosuppressive drugs.

Keywords: Inflammatory Bowel Disease; Regenerative Medicine; Mesenchymal Stem Cell

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Role of microRNAs in acute myeloid leukemia (Review)

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Introduction: Acute myeloid leukemia (AML) is an aggressive haematological malignancy characterized by abnormal proliferation and differentiation of immature myeloid cells. Despite a growing list of treatment options, most patients still relapse and die after remission, and the prognosis remains unideal. It is necessary to explore new biomarkers for diagnosis, prognostication, and therapeutic targets of AML so as to develop more effective surveillance and treatment programs. MicroRNAs (miRNAs) are small RNA molecules of approximately 22 nucleotides that bind to the 3′ untranslated region (3′-UTR) of the target mRNA and negatively regulate the expression of the target gene at the transcriptional level. miRNAs mainly participate in the pathogenesis of AML through the following five mechanisms: copy number alterations, change in the proximity to the oncogenic genomic region due to chromosomal translocation, epigenetic changes, aberrant targeting of miRNA promoter regions by altered transcription factors or oncoproteins, and finally, dysregulated miRNAs processing. This study's objective was to look at the role of microRNAs in acute myeloid leukemia.

Methods: This study on the role of microRNAs in acute myeloid leukemia used scientific databases including Science Direct, Springer, Google Scholar, and PubMed.

Results: Results showed Each AML subtype seems to exhibit a unique miRNA signature that distinguishes it from others. For example, Chen et al. reported that miR-9, an oncogenic miRNA, was overexpressed in the mixed lineage leukemia (MLL)-rearranged AML patients. Inhibition of miR-9 expression could significantly reduce cell growth/viability and promote apoptosis. Emmerich et al. found miR-9, significantly downregulated in pediatric AML with t(8;21), was characterized by its tumour-suppressive property. Upregulation of miR-9 decreased leukemic growth and induced monocytic differentiation of t(8;21) AML cell lines in vitro and in vivo. Functionally, miR-9 exerted its effects by binding to let-7 to suppress the oncogenic LIN28B/HMGA2 axis. In another study, miR-9-1 was observed to be downregulated in t(8;21) AML. Besides, overexpressed miR-9-1 induced differentiation and inhibited proliferation in t(8;21) AML cell lines. MiR-10a/b was significantly increased in AML patients with t(8;21), t(9;11), NPM1

mutation, and particularly M1, M2, and M3 subtype. Abnormal high expression in those patients led to unlimited proliferation of immature blood progenitors and repressed differentiation and maturation of mature blood cells. Another study showed that miR-10a overexpression was significantly associated with French-American-British (FAB)-M3/t(15;17) subtypes and NPM1 mutation, leading to a lower percentage of bone marrow (BM) blasts, while overexpression of miR-10b was correlated with NPM1 and DNMT3A mutations, resulting in a higher percentage of BM blasts. Some studies observed overexpression of the miR-181 in cytogenetic normal AML (CN-AML) patients with CEBPA mutations, FLT3-ITD, and/or wild-type NPM1 and t(15;17). MiR-155 was upregulated in FLT3-ITD-associated AML and targeted the myeloid transcription factor PU.1. Knockdown of miR-155 could repress proliferation and induce apoptosis of FLT3-ITD-associated leukemic cells.

Conclusion: In this review, we discussed miRNAs, involving subtypes, molecular function, chemoresistance and prognosis in AML, and the interactions between major ncRNAs. Currently, the role of miRNAs in AML is most studied, but the mechanisms of microRNAs in AML still remain complex and unclear owing to miRNA target genes ranging from tens to hundreds and involving different signaling pathways.

Keywords: microRNAs, Acute Myeloid Leukemia, Leukemic Cells, Oncogenic

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Role of microRNAs in producing and profiling of Induced Pluripotent Stem Cell (iPS) (Review)

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Introduction: MicroRNAs (miRNAs) are a group of non-coding RNAs that are approximately 22 nucleotides long.A known mechanism of their action is preventing the translation of mRNAs or destroying them. Several studies have investigated the expression profile of miRNAs in various cells, including stem cells. Expanding our knowledge in this area can be used to determine the differentiation state of cells, such as the pluripotency status of stem cells. This review aims to provide summarized information about the role of miRNAs in producing and profiling Induced Pluripotent Stem Cells (iPS) to gain deeper insight into this widely used and prominent area of cell-based studies and therapies.

Methods: This review was prepared by searching for up-to-date articles on websites such as Pubmed, Scopus, and Google Scholar using the following keywords. Articles corresponding to the specified criteria were selected.

Results: Some studies suggest the role of miRNAs in the specific characteristics of embryonic stem cells (ESCs), such as the ability to renew themselves through division and the potential to produce all cell types. Induced pluripotent stem cells (iPSCs) are another type of stem cell that researchers are focused on, which share many features with ESCs, such as pluripotency and the ability to differentiate into the cells of all three embryonic layers. These cells are created by reprogramming somatic cells and provide a common source of stem cells for various scientific purposes, from basic studies to cell-based therapies such as regenerative medicine. iPSCs, however, have a somatic donor memory that facilitates their redifferentiation into their origin tissue. One of the epigenetic role players in this feature is miRNAs, such as the role of miR-155 in keeping the memory of bone marrow-derived iPSCs toward hematopoietic progenitor cells. For generating iPSCs several methods can be applied to induce a defined set of genes which expression would lead to create embryonic stem cells. These techniques include the use of viral vectors carrying important genes such as Oct4, Sox2, Klf4, c-Myc, or Nanog to cause elevation of their expression. Researchers have attempted to demonstrate the differences between various miRNAs derived from different types of stem cells. Due to these investigations,

increased expression levels of a group of miRNAs, including miR-302 and 17-92 clusters are reported in the iPSCs and hESCs stem cells. It is shown that the treatment of cultured cells with selected microRNA mimics has improved the differentiation of somatic cells into iPSCs. In another study, fourteen miRNAs were identified, including miR-132 and miR-212, whose repression would lead to improved reprogramming of fibroblast cells and differentiation into iPSCs. The mentioned results are related to the deactivation of other epigenetic factors' inhibitors.

Conclusion: Expanding the database of miRNAome of stem cells will enable researchers to improve methods of classification, production, and assessment of the state and safety of iPSCs. This will allow the utilization of these stem cells with greater safety and efficacy in clinical purposes.

Keywords: Induced pluripotent stem cell, iPSC, reprogramming, MicroRNA , miRNAs

Role of miRNAs in Alzheimer's Disease (Review)

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease and it is the most common cause of dementia worldwide. It is characterized by neuronal death, loss of synaptic function, and atrophy in different brain areas, with consequent loss of cognitive functions and memory. AD is characterized by neuritic (or amyloid) plaques and neurofibrillary tangles (NFTs). Neuritic plaques are extracellular accumulations of beta-amyloid (Aβ). Many studies have suggested that Aβ regulates neuronal and synaptic activities. Its accumulation in the brain plays a crucial role in initiating the disease and triggering a complex pathological cascade, which leads to neuronal damage. Aβ peptide derives from the enzymatic proteolysis of the amyloid precursor protein (APP), a protein that physiologically plays an important role in brain homeostasis. The first pathway involved in APP processing is the non-amyloidogenic α-secretase-mediated pathway. APP cleavage by α-secretase generates sAPPα, a soluble molecule that has a probable neuroprotective function. Indeed, this peptide plays an important role in the plasticity and survival of neurons and in the protection against cytotoxicity. MiRNAs (or microRNAs) are small noncoding RNAs that play a significant role in the post-transcriptional regulation of gene expression in eukaryotes. The miRNAs exert their action in post-transcriptional gene silencing, binding to the coding region as well as the 3′ and 5′ untranslated region (UTR) of the messenger RNAs (mRNAs). The aim of this study was to investigate Role of miRNAs in Alzheimer's Disease.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The results of a number of studies are as follows: Higaki et al. conducted a study in order to correlate the differential expression of the miRNA-200 family (miRNA-200a, -141, -429, -200b, -200c) in the initial phases of AD in the mouse brain Tg2576. Tg2576 mice overexpress the APP protein (Swedish KM670/671NL mutation). Analysis of the total RNA microarray extracted from cortical tissues of mice revealed that miRNA-200a, -141, -429, -200b, and -200c were upregulated only in Tg2576 mice of 10 months of age. These results suggest that some miRNAs may respond to the early Aβ accumulation. In addition, an in vitro study was conducted on primary

murine neuronal cells (PMNC) isolated from the cortical tissues of mice in order to verify if the expression of miRNA-200b and miRNA-200c are altered in response to neuronal damage induced by Aβ1. The treatment with Aβ of the PMNC cells induced the upregulation of miRNA-200b or -200c. Subsequently, the cells were transfected with miRNA-200b/c demonstrating that the upregulation of miRNA-200b and miRNA-200c reduced the secretion of Aβ in the conditioned medium. In order to evaluate the effect of miRNA-200b/c in vivo, Tg2576 mice were treated with miRNA-200b/c by intracerebroventricular injection. This experiment confirmed what was obtained in vitro, suggesting that miRNA-200b and miRNA-200c may be potential therapeutic targets in AD. Liu et al. conducted a study to evaluate the expression of miRNA-220b, miRNA-135a, and miRNA-429 in the hippocampus of APP/PSEN1 transgenic mice. Microarray miRNA analysis showed that these miRNAs were significantly upregulated. In addition, this analysis was supported by bioinformatics tools that disclose the potential interaction between APP and BACE-1, an enzyme responsible for the production of Aβ.

Conclusion: level of Aβ and other proteins. MiRNAs may be a therapeutic target with great research potential in the current or a long period in the field of AD. In contrast to conventional drugs, miRNAs are highly targeted. MiRNAs can directly bind to the corresponding signalling pathways to regulate the expression of the target protein. However, miRNAs need to be administered systemically to the central nervous system to function in a large dose. It is difficult for them to pass through the blood-brain barrier, and their relative utilization is extremely low. Local brain drug delivery has significant effects in animal treatment research, while local brain drug delivery is difficult to achieve in current clinical treatments. In the future, when clinical drug delivery technology is further improved, local drug delivery is expected to be used to deliver miRNAs to the brain to treat AD.

Keywords: miRNAs, Alzheimer's Disease, signalling pathways

Role of Notch Signaling in Acute Leukemia Stem Cells (Review)

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Introduction: Leukemia is a group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These blood cells are not fully developed and are called blasts or leukemia cells. Notch has an important role in several functions related to embryogenesis and cell fate in adult tissues. Indeed, Notch signaling has been extensively linked to both processes of normal and malignant stem cell (SC) self-renewal. For this reason, it is important to comprehend its implications not only in its physiological form, but also in its aberrant variety. Our objective with this review is to summarize the available information about the hematological role of Notch, mainly in the regulation of the leukemic stem cells (LSCs) of acute myeloid leukemia (AML). In this paper, we also examine the interdependence of Notch signaling with Hedgehog (Hh) and Wnt. These 3 pathways are connected during embryo development, but also in SC regulation and differentiation in different tissues. The aim of this study was to investigate the role of Notch Signaling in Acute Leukemia Stem Cells.

Methods: This study used scientific databases including Science Direct, Springer, Google Scholar, and PubMed.

Results: Results showed A The important role of Notch in embryos was described by Robert-Moreno et al. when they studied Notch1 mutation in mouse embryos. They showed that a mutation in this gene entails deficiencies in intra-embryonic hematopoiesis. In adults, Notch has a crucial position in hematopoiesis: its inhibition can alter hematopoietic linages due to its importance in cell fate. Indeed, Notch1 has a major role in adult hematopoiesis by controlling events, such as lymphoid vs. myeloid differentiation, T vs. B lymphoid fate, αβ vs. γδ T-cell fate, and possibly CD4 vs. CD8 T-cell lineages. Furthermore, Notch, certainly Notch1 , is needed for the expansion of the hematopoietic stem cell (HSC) compartment. Almost 60% of patients with T-cell acute lymphoblastic leukemia (T-ALL) have mutations of NOTCH1 , but the prognosis of this mutation is not clear and seems to be dependent on additional genetic lesions. The high ratio of mutations in this gene suggest that T-ALL is the hematological neoplasia most closely related to this signaling pathway. In this neoplasia, NOTCH3 promotes JAG1, a phenomenon that is caused by a NOTCH3/JAG1 auto sustaining

loop. This mechanism would produce a positive auto feedback and a stimulant paracrine effect in the adjacent cells. The loop seems to support the survival, proliferation, and invasion of leukemic cells and contributes to the development and progression of T-ALL. Moreover, this signaling pathway could have prognostic value in those patients suffering from chronic lymphocytic leukemia (CLL). There are multiple studies that support NOTCH1 mutations as a negative predictor factor of CLL patients. Indeed, some authors found NOTCH1 mutated in 11% of CLL patients and found that mutations in this gene are in 90% of the cases mutually exclusive with TP53 disruptions, and confer a similarly dismal prognosis with a reduction in the overall survival (OS). Therefore, the role of Notch seems fundamental for lymphoid neoplasia.

Conclusion: In order to exploit the therapeutic potential of the Notch pathway, firstly, we believe it is essential to decipher the role of Notch in the regulation of the quiescence of the LSC population. Single-cell technologies might help us in this difficult task. In a further step, targeted therapies could be employed, either directed only towards Notch or also directed towards Hh and/or Wnt, alongside conventional chemotherapy. This therapeutic strategy could decrease the quiescence of LSCs, increase their chemo sensibility and achieve the eradication of LSCs and AML curation.

Keywords: Notch Signaling, Acute Leukemia, Stem Cells

Role of Notch Signaling Pathway in Glioblastoma Pathogenesis (Review)

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Introduction: The most prevalent and lethal primary brain tumor is glioblastoma. It is categorized as a Grade IV astrocytoma by the World Health Organization and accounts for 70% of all gliomas. Cell proliferation, apoptosis, stem cell maintenance, cell fate determination, and tissue homeostasis are just a few of the physiological and developmental activities that Notch signaling is essential. This system has been retained throughout evolution. Mammals have four homologous proteins called Notch1, Notch2, Notch3, and Notch4 that operate as cytoplasmic receptors and can bind the ligand families Jagged (Jagged1 and -2) and Delta-like (Dll1-3 and -4). They are single-pass transmembrane proteins, as are the receptors and ligands. The interaction between Notch and its ligands can occur in two ways: In trans, when they are present on neighbouring cells, or in cis when the receptor and ligand are present on the same cell. In the first case, binding leads to pathway activation, while in cis form interaction inhibits the signaling cascade. The aim of this study was to investigate the Role of the Notch Signaling Pathway in Glioblastoma Pathogenesis.

Methods: Scientific databases like Science Direct, Springer, Google Scholar, and PubMed were used for this review study.

Results: mRNA and protein levels of Notch1, Notch4, Dll1, Dll4, Jagged1, CBF1, Hey1, Hey2, and Hes1 are higher in brain tumor cells than normal brain cells, correlating with an elevated expression of VEGF and pAKT, and reduced levels of PTEN. In particular, Notch1 expression is higher in the survival of > 1-year patients than <1 year, whereas Notch1 overexpression is associated with low overall survival (OS), suggesting a controversial role of Notch1 in glioma genesis. Moreover, Notch1 is more expressed in peritumor-tissue GSCs compared to tumor-core GSCs. Notch1 and Notch4 levels correlate with those of GFAP and vimentin, respectively. Notch4 expression increases with higher-grade and primary tumors. Notch2 expression levels in Glioblastoma tissue correlate with stemness genes (nestin, SOX2), astrocyte fate genes (vimentin and GFAP), and anti-apoptotic proteins (BCL6 and BCL-W), but are inversely correlated with Olig2, CNP, and PLP1 (oligodendrocyte fate) and pro-apoptotic proteins (BAX and BCLAF1). The overexpression of Hey1, which is associated with survival and tumor grade, might be due to the

impairment of Notch and E2F signaling; it was demonstrated that its overexpression in NSCs triggers neurosphere formation and contributes to Glioblastoma proliferation [95]. On the contrary, several groups reported a weak expression of Notch1, Notch2, MAML1, and p300 in Glioblastoma. Intriguingly, the impairment of Notch signaling in secondary Glioblastoma, in which Hes1 expression is almost absent, is associated with the overexpression of ASCL1. On the other hand, the activation of Notch signaling in primary Glioblastoma is associated with low levels of ASCL1, suggesting that Notch inhibition via ASCL1 upregulation might be responsible for a potential progression into secondary Glioblastomas. Correlation between Glioblastoma molecular subtypes and Notch expression was also demonstrated. Concerning the mesenchymal subtype (the most aggressive one), Notch-related genes are the most highly enriched in high p-STAT3 patients, suggesting a synergy between Notch and STAT3 signaling. Verhaak et al. reported that Notch signaling is highly expressed in the classic subtype. The expression levels of Dll3 and Hey2 are low in proneural Glioblastomas, while the expression level of Notch1 is high.

Conclusion: Finally, even the non-canonical Notch pathway contributes to the development of gliomas. The findings demonstrated that Deltex1 (DTX1) levels were higher in glioblastoma than in healthy brain tissue, causing many pathways involved in glioma aggression, including RTK/PI3K/PKB and MAPK/ERK signaling, as well as the anti-apoptotic protein Mcl-1.

Keywords: Notch, Signaling Pathway, Glioblastoma, Pathogenesis

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Role of Nutrigenomics in Regulating the Expression of Genes Related to Type 2 Diabetes Mellitus (Review)

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Introduction: Type 2 diabetes mellitus (T2DM) is a disorder of blood glucose regulation, and is characterized primarily by a decrease in insulin secretion, typically accompanied by insulin resistance, The pathogenesis of DM is not completely understood, but nutrient-gene interactions at different levels, genetic, epigenetic, environmental, and lifestyle factors appear to be involved. The most common treatments for controlling diabetes focus on glucose control as a means to reduce long-term complications.

Methods: dietary management has shown to be a cornerstone modality in the attainment of good glycemic control in diabetes, Nutrients and dietary patterns are central issues in the prevention, development and treatment of this disease, and Nutrition/Diet remains a key player in diabetes prevention and management. variety of habits and environmental factors, including foods and natural componds affect the expression of genes involved in glucose transport, insulin secretion, antioxidant effects, inflammation, vascular functions and lipid metabolism.

Results: Although it is clear that both nutrients and genes play a distinct role in determining health, the complex interactions among genes, diet, and downstream networks are not well understood, Therefore, it has become necessary to understand how nutrients act at the molecular level which in turn involves a cascade of nutrient-related interactions at the gene, protein and metabolic levels. The promise of nutrigenomics is of personalized nutrition that will lead to optimization or maintenance of good health and/or prevention of the development of chronic diseases. food-derived bioactive compounds

significantly influence changes in the genome, epigenome, proteome and metabolome.

Conclusion: The aim of the present review was to provide insights of the role of gene variants and nutrient interactions, the importance of nutrients and dietary patterns on coding genes and their functions and how epigenetic changes can alter cellular signaling in response to nutrients and the dietary interventions that may help to management the onset of DM.

Keywords: Type 2 diabetes; Insulin Resistance: Nutrients: Dietary patterns: nutrigenomic; Gene-Nutrient Inte

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Role of P53 in Brest Cancer progression and therapy method (Review)

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Introduction: The tumor suppressor protein p53 as a guardian of the genome plays a crucial role in preventing cancer by inducing apoptosis, DNA repair, and cell cycle arrest. Dysregulation of p53, often through mutations or inhibitory interactions, contributes to the development of breast cancer. Notably, the transcription factor KLF12 and the negative regulator MDM2 are implicated in disrupting p53 function, leading to breast cancer initiation and progression. Another factor is BAG2 which plays a pivotal role in promoting the formation and propagation of mutant p53 aggregates. Elevated BAG2 levels are associated with relapse and poor prognosis in breast cancer patients.

Methods: Elevated BAG2 levels are associated with relapse and poor prognosis in breast cancer patients. These aggregates, in turn, hinder the mitochondrial apoptosis pathway, contributing to chemoresistance. Furthermore, the ubiquitin ligase RNF187, a member of the RING family, directly targets p53 for ubiquitination, perturbing its interaction with MDM2 and promoting breast cancer growth.

Results: Moreover, our findings suggest that BAG2 represents a potential therapeutic target for addressing drug resistance and enhancing chemotherapy efficacy in breast cancer patients, particularly those facing chemoresistance challenges. In conclusion, this review sheds light on the intricate interactions and mechanisms governing p53-associated breast cancer development and resistance, offering insights into strategies for potential therapeutic interventions.

Conclusion: In this review article, we delve into the various strategies investigated for addressing p53 mutations and their potential as treatments. These encompass distinct types of treatments that the efficacy and constraints of these strategies within both pre-clinical and clinical contexts are explored and discussed comprehensively.

Keywords: Breast cancer, p53, Treatment, Tissue

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Role of Stem Cells in Metastasis in Ovarian Cancer (Review)

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Introduction: Ovarian cancer with 22,240 new cases reported in the United States each year, ovarian cancer (OC) is the most common cause of mortality from gynecologic malignancies. Metastasis is a common problem in OC treatment because it is believed that 75% of OC patients had disseminated illness in the peritoneal cavity at the time of initial diagnosis. Although this treatment is initially successful, the five-year survival rate is only about 30% and up to 80% of women with advanced-stage ovarian high-grade serous carcinoma (HGSOC) relapse with metastatic cancer. According to the CSC theory, a subset of malignant cells exists within a tumor that is more likely to self-renew, produce a variety of tumour-related cells, and support carcinogenesis. The aim of this study was to investigate the Role of Stem Cells in Metastasis in Ovarian Cancer.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Multiple studies have shown ascites to be a rich source of OCSCs. This non-adherent microenvironment is lethal to adherent tumors cells, and only cells with mesenchymal features can tolerate the anoikis stress and survive. Ascites contains a variety of tumour-promoting soluble factors that contribute to CSC enrichment, such as interleukin (IL)-6, IL-8, IL-10, osteoprotegerin, vascular endothelial growth factor (VEGF), and extracellular vehicles (EVs) . We recently reported that IL-6 regulates stemness features of CSCs by activating STAT3 signaling and enhancing ALDH1A1 expression. In addition, several studies have emphasized the importance of EVs in promoting cancer progression, which adds another level of complexity to study the microenvironment of ascites. Runz and colleagues identified CD24 and EpCAM as cargo proteins of exosomes in cell lines and malignant ascites, which are both stemness and prognostic markers of OC. Other molecules carried by EVs reported in OC include L1 adhesion molecule (CD171), activated leukocyte cell adhesion molecule (ALCAM), CD44 and claudin-4. Given the variety of potential factors contributing to CSC maintenance, ascites is considered to promote the acquisition of the stem cell state. Floating OC cells travel along with the ascites, with the movement of respiratory force, before settling onto the new sites. Adhesion to mesothelium, the lining of the peritoneal cavity, is the first step of implantation. This step is

facilitated by CD44 and β1 integrin heterodimers on the surface of floating OC cells, which are ligands for hyaluronic acid (HA) and the extracellular matrix molecules on mesothelial cells. Intriguingly, mesothelial cells facilitate cancer stemness properties in spheroids of OC cells, including increasing CD44 expression, suggesting a positive feedback loop in the adhesion step between mesothelium and floating OC cells.

Conclusion: It is notable that the CSC population within a tumor is not a uniform collection of cells. Cell division is made possible by the asymmetric division that distinguishes CSCs. Additionally, the dynamic coexistence of CSC in quiescent, proliferative, and metastatic phases may activate several signaling pathways, leading to therapy failure with a single conventional treatment. In order to address heterogeneity, a recent study developed patient-derived OC organoid culture systems. Organoid lines were xenografted to the main tumor to capture the intratumoral and intertumoral heterogeneity of the tumor. This cutting-edge technology has a lot of potential for customized OCSC-based therapeutics. Another obstacle is the small therapeutic window that results from CSC-directed therapy's lack of specificity compared to regular stem cells. For instance, it has been demonstrated that blocking BET has an impact on intestinal stem cells, resulting in GI toxicity and a disruption of tissue homeostasis in numerous organs. Target selection is required due to biological distinctions between CSCs and regular stem cells that prevent off-target effects. A more effective intervention would be made possible by significant developments in delivery technologies, such as the use of nanoparticle-mediated strategies and oncolytic viruses that only multiply in cancer cells. Together, minimizing side effects related to targeted therapy and enhancing pharmacological efficacy are crucial. The creation of the ideal timing for administering CSC-targeted treatment and the emergence of resistance are additional difficulties. The greatest benefit to patients may come through early CSC intervention, either prior to or concurrently administered with chemotherapy.

Keywords: Stem Cells, Metastasis, Ovarian Cancer

Role of Stem Cells in Metastasis in Ovarian Cancer (Review)

mahdie balavar,[1,*]

1. ISLAMIC AZAD UNIVERSITY OF FALAVARJAN BRANCH

Introduction: Ovarian cancer with 22,240 new cases reported in the United States each year, ovarian cancer (OC) is the most common cause of mortality from gynecologic malignancies. Metastasis is a common problem in OC treatment because it is believed that 75% of OC patients had disseminated illness in the peritoneal cavity at the time of initial diagnosis. Although this treatment is initially successful, the five-year survival rate is only about 30% and up to 80% of women with advanced-stage ovarian high-grade serous carcinoma (HGSOC) relapse with metastatic cancer. According to the CSC theory, a subset of malignant cells exists within a tumor that is more likely to self-renew, produce a variety of tumor-related cells, and support carcinogenesis. The aim of this study was investigating Role of Stem Cells in Metastasis in Ovarian Cancer.

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Keywords: Stem Cells, Metastasis, Ovarian Cancer

Role of the Extracellular Matrix with HA in Ovarian Cancer (Review)

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Introduction: The most prevalent cancer and the sixth most common reason for cancer-related death in women worldwide is ovarian cancer. Depending on the tissue in which it is located, HA is a big polymer that extrudes into the extracellular space and is composed of repeated N-acetyl glucosamine and D-glucuronic acid disaccharides of varied molecular weight and size. The World Health Organization (WHO) classifies ovarian neoplasms according to their histological differentiation, namely epithelial, sex cord-stromal and germ cell neoplasms. Epithelial ovarian tumors represent the largest group and are basically subdivided into serous, mucinous, endometrioid, clear cell and transitional cell tumors; the latter including Brenner tumors. Among these groups of tumors, three categories are distinguished according to their biological behaviour: benign, borderline and malignant. Several rare malignant neoplasms complete the category of epithelial ovarian tumors, such as mixed carcinoma, carcinosarcoma and undifferentiated carcinoma. This study sought to understand how the extracellular matrix and ha function in ovarian cancer.

Methods: This review study has written the role of the extracellular matrix with ha in ovarian cancer from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Results have indicated Tumors can significantly alter the composition and structure of the matrix by interfering with the regular regulation of ECM production. The physiological function of HA varies significantly depending on HA size, the presence or absence of HA binding proteins, and the presence or absence of cell surface receptors. Alterations in the expression of several ECM molecules, including hyaluronan (HA) and CD44, have been described in ovarian cancer and have an impact on the outcome of the disease. HA is highly abundant in several cancers. The stroma surrounding the tumor or the tumor cells themselves may have higher HA levels. In ovarian cancer tumor models, increased HA has been found to be highly associated with the level of invasiveness and metastatic potential.

Conclusion: Ovarian cancer cells are surrounded by a peritumoral stroma that is rich in HA and CD44, which can encourage the tumour's ability to

spread. Further investigation is necessary since these compounds show potential as therapeutic targets for ovarian cancer.

Keywords: Extracellular Matrix, HA, Ovarian Cancer

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Role Play in Medical Education: A Review on Current Evidence (Review)

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Introduction: Visionary teaching-learning strategies are necessary to facilitate community orientation and boost cognition of the social determinants of health among millennial trainees in the health professions. One of these strategies is role-playing. Role-playing is a powerful and active learning method through which students and teachers present lessons dramatically to others. Hence, students cooperate more in learning. The importance of this method is to improve professionalism among trainees in medical sciences.

Methods: Authors scoped to determine the impact of role-playing in medical education. For this purpose, we searched systematicaly in "PubMed", "Scopus", and "Web of Science".The keywords in this search were "role-playing", "medical education". This review aimed to examine the impact of role-playing on Medical Education output.

Results: Studies have shown that the role-playing as a teaching method, helps trainees upgrade their communication skills, helps doctors to understand patients' behavior and doctors' reactions, improves counseling for resident doctors, bridges the gap between teaching and learning, promotes insight among students in patients and therapists' roles in mental health, and strengthen clinical reasoning. Although role-playing has a crucial impact on health promotion, it enhances the realism of trainees, develops community practice and motivation of students, improves the practical skills of trainees, recognizes patients' issues, and provides long-lasting lessons.

Conclusion: Based on the colossal medicine program, performing role-playing for all lesson titles was neither enforceable nor wise. Thus, role-playing should be implemented in lessons such as Family Medicine and Medical Genetics and in topics where trainees should learn to communicate with patients. Another critical point of role-playing is the enhancement of the Communities of Practice (CoP), including students in practice more than ever before and training more empowered clinicians.

Keywords: role playing, medical education

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rs201365744 promotes lung adenocarcinoma by disturbing interactions of LCN2 protein: an in- silico approach (Research Paper)

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Introduction: Lung cancer remains the leading cause of cancer related deaths worldwide despite the advancement in screening, diagnosis, and treatment. Among different sub-types of lung cancer, lung adenocarcinoma (LUAD) has become the most prevalent one. One of the challenges in the treatment of LUAD is early diagnosis to increase survival rate. Over the years, molecular methods such as DNA microarrays have been developed to have better insights into the biology of lung cancer. Moreover, using reliable biomarkers such as single nucleotide polymorphisms (SNP) would immensely improve prognosis of the disease. Thus, this study aimed to identify novel SNPs affecting protein interactions by means of bioinformatics tools.

Methods: NCBI Gene Expression Omnibus database (GEO) was used to obtain GSE136043, which was analyzed using GEO2R online software to identify differentially expressed genes (DEG). Genes with logFC > 3 and adjusted p-value < 0.01 were selected and validation was performed by GEPIA2 and ENCORI online soft wares. One of the most significant up-regulated genes, Lipocalin 2(LCN2), was chosen for further analysis. Signaling pathway of the selected gene was achieved using Kyoto Encyclopedia of Genes and Genomes (KEGG). Next, SNPs in coding sequence (CDS) for LCN2 were extracted from NCBI dbSNP database and then taken to SIFT (a sequence homology-based tool) to identify deleterious SNPs. Biophysical validation of these SNPs was performed using HOPE web server.

Results: According to GEO2R analysis, LCN2 was one of the most significant up-regulated genes (logFC = 5.17, adjusted p-value = 0.0002). Results from GEPIA2 showed that overexpression of LCN2 in LUAD is significant (p-value < 0.05). This was further validated by ENCORI using gene differential expression tool (p-value = 4.6e-10, FDR = 3.2e-9). Results from KEGG showed that LCN2 is involved in Interleukin 17 signaling pathway, as well. 21 deleterious SNPs were identified in the coding region using SIFT. Three SNPs with the highest SIFT score were taken to HOPE web server to ensure that the mutation would change protein interactions. It was revealed that

rs201365744 is the most significant deleterious SNP in the protein coding region of LCN2. In this SNP, Tyrosine mutates into Histidine at position 76. Based on the data achieved from HOPE, the mutant residue is smaller and more hydrophobic than the wild-type residue. The changes in size and hydrophobicity will affect formation of hydrogen bonds. Since the mutated residue is situated in a domain that is essential for binding of other molecules and is in contact with residues in a domain that is also important for binding, the mutation can alter the interactions between these domains, which can disturb function of the protein, subsequently.

Conclusion: According to results of this study, rs201365744 can promote LUAD development by changing interactions and function of LCN2, which can act as a potential biomarker in prognosis of lung adenocarcinoma.

Keywords: Cancer, LUAD, LCN2, Single nucleotide polymorphism, Microarray

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Safety assessment after delivering drugs across the blood-brain barrier using Rapid Short-Pulse sequences in vivo (Research Paper)

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Introduction: Focused ultrasound and microbubbles can alter the blood-brain barrier (BBB) permeability, allowing drugs to enter the brain. However, when using long ultrasound pulses (10 ms), the BBB remains open for several hours or days, which allows unwanted bloodborne proteins, such as albumin and immunoglobulins, to enter the brain and trigger a neuroimmune response (i.e., activation of microglial cells). Recently, we have developed a Rapid Short-Pulse (RaSP) ultrasound sequence that alters the BBB permeability more uniformly throughout the brain and for less than 10 minutes. Here, we explored whether the shorter duration of BBB disruption is representative of a safer delivery profile. We therefore evaluated whether the RaSP sequence reduces albumin and immunoglobulin extravasation and whether the neuroimmune system remains inactive.

Methods: We applied a RaSP sequence (pulse length: 5 cycles, repetition frequency: 1.25 kHz) or ms-long sequence (10,000 cycles; 0.5 Hz) onto the left murine hippocampus (1 MHz, 350 kPa, n = 5). Fluorescent 3 kDa dextran, our model drug, was systemically administered before the injection of SonoVue® microbubbles. Brains were extracted and sectioned either 0, 10 or 20 min after the ultrasound treatment to assess the extent of albumin and immunoglobulin extravasation; or 0, 2, 24 or 48 h after ultrasound exposure to investigate the involvement of microglia and astrocytes, both via immunofluorescence staining

Results: Although the RaSP sequence deposited 150 times less acoustic energy into the brain than long pulses, a similar dextran dose was delivered to the brain. Whereas long pulses resulted in albumin extravasating into the brain at all the time points tested, the RaSP sequence resulted in 3.7-fold less albumin extravasation at 0 min and an undetectable level of albumin at 10 and

20 min. With the RaSP sequence, no immunoglobulins were detected at all time points. Also, staining revealed that the RaSP sequence produced no uptake of the model drug within microglia and astrocytes, while with long pulses the microglia showed higher uptake and had a more rounded shape, a sign of activation. These results indicate that RaSP sequences can deliver drugs to the brain with a nearly negligible level of BBB disruption and neuroimmune response.

Conclusion: Safety features of RaSP and ms-long pulse sequences was confirmed.we demonstrated Less albumin and no immunoglobulin extravasates into the brain at 0, 10 and 20 min after ultrasound emitted in a RaSP sequence and Little or no uptake of dextran at 0, 2, 24 and 48 h in microglia and astrocytes, shows less of an immune response.

Keywords: Blood-Brain Barrier, Drug Dlivery, Focused Ultrasound, Rapid Sh

Saffron (Crocus sativus L.) in combination with resistance training reduced blood pressure in the elderly hypertensive men (Research Paper)

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1. University of Tehran, dept of Exercise Physiology

Introduction: The mechanisms and causes of hypertension, especially essential hypertension, are not fully understood. Several factors, such as atherosclerotic plaques and inflammation, aging and disease, and poor diet and inadequate physical activity, are among the factors implicated. In addition to the treatment of hypertension with standard medications, adjuvant therapies are needed to improve patient outcomes and mitigate potential side effects of treatment strategies. To date, there is accumulating data on the effect of exercise with or without other treatments such as herbal remedies on cardiovascular risk factors. So, we sought to determine the independent and combined effects of saffron and resistance training on markers of cardiovascular risk factors in elderly hypertensive patients.

Methods: 48 Hypertensive older men were randomly assigned to a control group (C) or one of three experimental groups [saffron consumption (S), resistance training (R), and resistance training + saffron (RS)] for 12 weeks. cardiovascular risk factors were measured at baseline and following the 12-week intervention period. Patients in S and RS received one tablet containing 200 mg of saffron daily. Primary outcomes were analyzed using univariate analysis of covariance (ANCOVA).

Results: In comparison to the CO and S, RTS reduced systolic BP. Nitric oxide increased in the RTS compared to the CO group. There was a significant increase and decrease in adiponectin and endothelin-1 in the S and RT compared to the CO, respectively.

Conclusion: Overall, the present study indicates that 12 weeks of resistance training and saffron supplementation, when combined, effectively improves cardiovascular risk factors in older hypertensive male patients. We also observed some positive effects for S alone and R alone in increasing HDL, recommended for patients who were unwilling or unable to do one or the other. In general, our findings could lead to future research questions to find out the mechanisms involved in the effects of resistance training or saffron supplementation on how changes in vascular endothelium and its

cardiovascular healing consequences and mechanistic changes in some lesser-known inflammatory biomarkers.

Keywords: elderly men, hypertension, resistance training, saffron

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Safranal, a natural cyclical terpenic aldehyde from Crocus sativus, induced toxic effects on human gastric cancer cells (Research Paper)

Nazanin Shadanpour,[1] Fatemeh B. Rassouli,[2] Parastoo Azadbeigie,[3] Farhang Haddad,[4,*]

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3.
4.

Introduction: Saffron is spice derived from the dried red-dark stigmas of Crocus sativus, and safranal (C10H14O) is one of its major constituents. As a natural cyclical terpenic aldehyde, safranal has several pharmaceutical activities such as anti-oxidative, neuroprotective and anti-cancer effects. Cytotoxic effects of safranal against leukemia, prostate, cervix, lung and hepatocellular carcinomas were mediated through various mechanism including mitochondrial dysfunction and DNA fragmentation. Gastric cancer is the fourth most common cancer in the world, while more than 50% of cases occur in the Eastern Asia. Although the incidence and mortality rates are slowly declining in many countries, gastric cancer still remains a significant public health problem. The present study was designed to assess toxicity of safranal on human gastric cancer cells.

Methods: To determine cytotoxicity of safranal, MKN-45 cells (a human gastric adenocarcinoma cell line) were treated with 1.6 mM and 3.2 mM of safranal. After 24, 48, 72, 96 hours, cell viability was determined by alamarBlue assay as a colorimetric method. In addition, viability of HFF-3 cells (human fibroblasts) were also evaluated upon treatment with the same concentrations of safranal.

Results: Assessment of MKN-45 cell viability after treatment with safranal revealed that this agent induced toxicity in a dose-dependent manner. Our results showed that viability of MKN-45 cells after 24, 48, 72 and 96 hours treatment with 1.6 mM safranal were as 100%, 97.4%, 89% and 64.85%, respectively. Moreover, MKN-45 cell viability were determined to be 95%, 91.7%, 79% and 45.29% after 24, 48, 72 and 96 hours treatment with 3.2 mM safranal, respectively. In addition, safranal induced toxic effects on normal cells as well, since 81% and 61.2% of HFF-3 cells were alive upon 72 hour treatment with 1.6 mM and 3.2 mM safranal, respectively.

Conclusion: Taken together, our findings indicated toxic effects of safranal on human gastric adenocarcinoma cells and fibroblasts. More research must be done to deeply understand the mechanism of safranal toxic action.

Keywords: Safranal, Crocus sativus, cytotoxic, gastric cancer, alamarBlue assay

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Saliva is a reliable diagnostic biomarker and potent stem cell provenance for Alzheimer's Disease. (Review)

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disease that causes progressive dementia. AD is the most prevalent type of dementia; approximately 60% - 80% of cases are over 65 years old. Currently, cerebrospinal fluid (CSF) assessment is applied for AD diagnosis, which later in the disease process has good diagnostic precision. However, recent studies proposed that human saliva could be a reliable biofluid for the early diagnosis of many diseases, including oral diseases, cancer, diabetes, and brain disorders. In addition, it potentially has prognostic and therapeutic value for patient monitoring.

Methods: It is necessary to develop a sensitive and noninvasive method for early diagnosis and monitoring of AD. The saliva has been introduced to be a good candidate as a circulating biological marker for AD. The saliva has specific features, including early, cost-effective, noninvasive, safe, and stable diagnostic biomarkers. Moreover, it can be considered for screening in large populations. However, neuroimaging biomarkers are expensive and cause radiation. Most compounds discovered in blood can pass into the saliva via passive diffusion, active transport, or microfiltration.

Results: In addition, salivary glands contain stem cells with AD biomarkers and potentially sensitive cellular biomarkers for cell-based regenerative medicine. Although stem cells derived from aged salivary glands may be decreased in number, they maintain their stemness features in comparison to the stem cells harvested from young salivary glands, proposing that the salivary glands remain as a vital source of stem cells that are applicable for combat age-related disorders. Previous studies described some valuable diagnostic biomarkers for AD, like amyloid beta 1-42 (Aβ42) and tau, but lactoferrin and selected metabolites also have potential. It seems saliva studies named saliva omics can be preferable over the other invasive methods and are still a new research area that needs more studies.

Conclusion: Finding a peripheral biomarker with validated detection will identify high-risk cases, facilitating early initiation of treatments that may prove more effective therapeutics approaches such as stem cell transplantation.

However, some limitations must be resolved before clinical studies, including regulating the host immune response and potential tumorigenesis arising from transplantation. Since saliva is affected by many exogenous factors, some inflammatory markers may be impacted by various simultaneous disorders. This subject is critical for dentists to exclude oral diseases that may dramatically affect salivary levels.

Keywords: Saliva, Biomarkers, Alzheimer Disease, Stem Cells, Regenerative Medicine

Salmonella-mediated cancer therapy: a therapeutic candidate for glioma (Review)

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Introduction: One of the most dangerous diseases in the world is cancer, and it is predicted that by 2030, more than 26 million people will be severely at risk of contracting it. The most common malignant tumor of the central nervous system is glioma, and 50% of patients suffer from its most aggressive type, glioblastoma. Despite recent advances in chemotherapy and surgical techniques, median survival rates are still consistently low. At the end of the 19th century, Wilhelm Bosch and William Coley discovered that live bacteria might cause tumor regression and increase patient survival, which led to the introduction of bacteria-mediated cancer therapy.

Methods: Today, it is known that the gram-negative bacterium Salmonella can be qualified as a candidate for cancer therapy. However, this bacterium can have severe side effects, which are chiefly related to its lipid A endotoxin, which is the product of the msbB gene. By deleting virulence genes of Salmonella, its complications can be reduced, but this should be done in such a way that it maintains a high affinity for solid tumors. In the new strain of this bacterium, two targeted deletions have been made in the region of msbB and purM genes, which have led to a decrease in lipid A toxicity and dependence on purine supplementation, respectively. Moreover, this new strain contains a non-synonymous single nucleotide polymorphism in the cheY gene, which reduces its capacity for chemotaxis. This gene present in the CheA/CheY two-component system, which is crucial for the motility and spread of bacteria in the tumor, as well as the chemotaxis response. However, studies showed that tumor colonization was not affected by the absence of CheY protein.VNP20009, which is a modified and new strain of SalmonellaTyphimurium, is significantly more capable of multiplying in tumors than in healthy tissues. Also, mutated Salmonella has the ability to enter the deep areas of tumors where common drugs cannot reach. In Salmonella infection, toll-like receptors (TLRs) that can recognize the molecular patterns of Gram-negative bacteria are first activated, then the host's immune system

is stimulated and antitumor activities are developed. After infection, a cascade of cellular signals is activated that triggers a storm of cytokines and chemokines, followed by an influx of immune cells into tumor tissues. Tumor cells that were damaged by Salmonella infection release ATP, which causes the activation of NLRP3 inflammasome and increases IL-1β, IL-18, and TNF-α, which are inflammatory cytokines and lead to tumor regression. Inflammasome activation can occur directly by Salmonella LPS or by ATP signals and phagocytosis of damaged tumor cells.

Results: Salmonella was first used in preclinical studies in 2000 for the treatment of advanced tumors but was discontinued in the first phase of clinical trials due to low tumor regression and the occurrence of side effects at high doses. However, intravenous infusion of VNP20009 increased circulating pro-inflammatory cytokines and caused significant colonization in tumor biopsies of 12% of patients. Therefore, with more research on the weaknesses of previous trials, the results of future clinical trials will be different and better. One of the obstacles that effect on the ability of VNP20009 in tumor targeting is a point mutation in the cheY gene. By replacing the mutant cheY with its wild-type sequence, the chemotactic ability of this strain was increased with an efficiency of 69%.In addition, by restoring the msbB gene in VNP20009 CheY+, optimization has been done, which has increased the chemotactic mobility. Another method that helps Salmonella to target tumors is to induce surface modifications in this bacterium, such as the display of arginine-glycine-aspartate (RGD) peptide sequences in the outer membrane protein A of Salmonella Typhimurium. Through this peptide, Salmonella can effectively bind to αvβ3, which is present in most tumor cells.

Conclusion: In conclusion, modified Salmonella has significant potential for bacteria-mediated cancer therapy. Many strains of Salmonella have so far been demonstrated to successfully reduce the growth of tumors when used in conjunction with other treatments.

Keywords: Salmonella Typhimurium, Glioma, Inflammasome, CheY gene

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Screening and prediction of diabetes using retinal images by artificial intelligence (Research Paper)

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Introduction: Diabetes is a metabolic disorder that leads to complications including cardiovascular renal and eye disease. Diabetes is a significant and costly heath problem in the world and is growing in incidence at almost epidemic levels. New and innovative ways of identification diagnosis treatment and follow up are needed to manage this growing problem. Using the retina and its blood vessel characteristics can provide a window into several disease processes. morphological characteristic the change in the venous or arterial vessel diameter especially in proximity to the optic disc allows the application of image analysis and automated classification in risk assessment of diabetes disease. Detection of width changes in blood vessels of the retina may be indicative of eye or systemic disease.

Methods: In order to detect vessel width change vessels must first be identified in available digital images. Extraction algorithms generally use exploratory techniques. They are faster computationally and usually determining useful morphometric information as part of the discovery process. Since the vessel boundaries are part of the discovery process these algorithms generally contain information such as vessel widths center points, and local orientation. at width change detection would need to follow three basic steps. The first step is to find the vessels in each image with the boundaries being identified to subpixel accuracy. Second is the step of transforming all vessels into the same coordinate system and identifying corresponding vessel pieces. Last is the ability to measure to subpixel accuracy the vessel widths and to identify changes in width over time. By using the DBICP registration algorithm, it is possible to determine transformations that can be used to accurately align both images as well as results generated from these images. Once final blood vessel boundary locations are determined, it is then possible to transform images into common coordinate systems through the process of registration. Once registered

widths can be compared utilizing the described hypothesis test framework attributing any change of 5 percent or less to normal vessel changes caused by the cardiac rhythm. For an experimental study a fixed number of subjects with known disease and a fixed number of no diseased subjects are selected and the diagnostic test is applied to both categories. This is a low-cost design useful for early stages of development of a new test.

Results: A preliminary validation of this software showed a sensitivity and specificity of 80 percent for the detection of normality based on precise detection of individual lesions. Decisions that depend on the detection of lesion patterns such as clinically significant macular edema showed a sensitivity and specificity of more than 95 percent. Validation by two expert graders suggested a sensitivity and specificity of below 90 percent for any lesion and of more than 95 percent for predicting overall retinopathy grade. The features of this system include high operating speed, performing a large number of samples at the same time the ability to send images to remote locations etc.

Conclusion: Such of the clinical investigation related to retinal vascular geometry has focused on hypertension and cardiovascular disease but less attention so far has been given to other systemic diseases such as diabetes. Early unpublished findings in diabetic patients suggest that retinal vascular geometry may also yield clinically useful information here. Such developments offer the prospect of a highly automated screening tool suitable for centralized analysis of retinal photographs captured locally using existing digital fundus cameras for example during routine examinations by optometrists. Such an arrangement might offer a highly cost effective opportunity to screen large populations for risk factors in a range of systemic diseases.

Keywords: Diabetes, Retinal image, Artificial intelligence, Telemedicine, vascular geometry

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Secretions Released From Menstrual Blood Derived Stem Cells Facilitate Spermatogenesis Restoration in Busulfan-Induced Non-obstructive Azoospermic Mice (Research Paper)

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Introduction: Nonobstructive azoospermia (NOA) is one of the most severe forms of male infertility, with limited treatment options. The aim of this study was to investigate whether the administration of Menstrual blood-derived stem cell secretome could promote spermatogenesis restoration in the busulfan-induced NOA mice model.

Methods: 18 adult mice were divided into three experimental groups: (1) Sham, (2) no treated group (NOA model), and (3) NOA+secretome administration. Secretome was obtained from menstrual blood mesenchymal stem cells (MenSCs). Ten microliters of secretome were first injected into the rate testis space in mice with NOA. Then, they received 500 microliters once a week for eight consecutive weeks intraperitoneally. Afterward, the animals were euthanized, and testis samples were taken for further evaluation.

Results: The spermatogenesis recovery was seen in secretome-administered groups in NOA mice that were confirmed by semen analysis and histopathological studies. Furthermore, the results showed that expression of DAZL, Vasa, Stra8, and Sycp3 was significantly increased in the secretome received group compared with the non-treated group, as demonstrated using quantitative real-time polymerase chain reaction.

Conclusion: In summary, our results indicated that the secretome of MenSCs could significantly facilitate spermatogenesis restoration of busulfan-induced NOA mice through paracrine activities.

Keywords: Nonobstructive azoospermia, menstrual blood stem cell, secretome, paracrine activity

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Serum Brain-Derived Neurotrophic Factor (BDNF) in COVID-19 Patients and its Association with the COVID-19 Manifestations (Research Paper)

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Introduction: COVID-19 is a systematic disease that frequently implies neurological and non-neurological manifestations, predominantly by inducing hypoxia. Brain-derived neurotrophic factor (BDNF) is a critical factor in regulating functions of the nervous and respiratory systems and has been strongly related to hypoxia. Therefore, this study planned to investigate BDNF association with COVID-19 manifestations primarily neurological impairments and infection-induced hypoxia.

Methods: We enrolled sixty-four COVID-19 patients and twenty-four healthy individuals in this study. Patients were divided into two groups, with and without neurological manifestations, and their serum BDNF levels were measured by enzyme-linked immunosorbent assay (ELISA).

Results: COVID-19 patients had significantly lower BDNF levels than healthy individuals (p=0.023). BDNF levels were significantly lower in patients with neurological manifestations than in healthy individuals (p=0.010). However, we did not observe a statistically significant difference in BDNF levels between patients with and without neurological manifestations (p=0.175). BDNF levels were significantly lower in patients with CNS manifestations (p=0.039) and higher in patients with fever (p=0.03) and dyspnea (p=0.006). Secondly, BDNF levels negatively correlate with oxygen therapy requirements (p=0.015).

Conclusion: These results strongly suggest the critical association between dysregulated BDNF and hypoxia in promoting COVID-19 manifestations, particularly neurological impairments.

Keywords: COVID-19, BDNF, Neurological manifestations, Hypoxia, Dyspnea.

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Sexual satisfaction predictors in women with cyclic mastalgia: a descriptive-analytical study (Research Paper)

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Introduction: There is a relationship between chronic pain and the quality of sexual life and, as a result, sexual dissatisfaction. Therefore, this study was conducted with the aim of determining the predictors of sexual satisfaction.

Methods: This is a descriptive-cross-sectional study that was conducted in 2022 on 204 women suffering from cyclic mastalgia referring to four comprehensive health centers and clinics of Kausar Hospital in Qazvin city. The study tools included theVisual analog scale and the Cardiff Clinic breast pain chart to diagnose cyclic mastalgia and Larson's sexual satisfaction evaluation questionnaire. Data were analyzed with SPSS version 23 software.

Results: The average age of the sample and their husbands was 33.05 ± 6.145 and 36.21 ± 5.973 years, respectively. Variables of social support, husband's interest in breast touching, woman's interest in wife, sexual behavior, were predictors of sexual satisfaction in sample people ($p<0.05$)). The findings showed that for each unit increase in the variables of husband's interest in touching the breast, woman's interest in her husband, social support and sexual behavior, the amount of sexual satisfaction increases by 0.23, 0.31, 0.09, and 0.25 respectively.

Conclusion: Social support, woman's interest in husband, husband's interest in breast touching, sexual behavior are predictors of sexual satisfaction in patients with cyclic mastalgia. Therefore, it is suggested to carry out interventions keeping in mind the mentioned cases in order to improve sexual satisfaction and subsequently increase the quality of sexual life of these women.

Keywords: Mastodynia, sexual health, predictors

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Signaling pathway-based Drug Repurposing approach a tool for treatment of breast cancer (Review)

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Introduction: Breast cancer is as one of the leading causes of malignant morbidity and cancer-related mortality among women worldwide. Signaling pathway play vital role in cell growth, proliferation and survival of breast cancer. Also, dysregulated signaling pathway is linked to poor treatment outcomes. Drug repositioning or repurposing is a promising field in drug discovery approach that identifies already-approved or investigational drugs to new diseases. Thus, this review provide a general overview of the anti-cancer mechanisms of drugs repurposed on the signaling pathways of breast cancer.

Methods: Several strategies have been used to identify drug repurposed effect on the signaling pathway in breast cancer with the "Drug repurposing" OR "Drug repositioning" AND "Breast cancer" AND "Signaling pathway" keywords which cited in Pubmed and Google scholar from 2015-2023. Finally, 21 included and 79 excluded articles were extracted from 100 paper published.

Results: A Several studies reveals that 30 drugs repurposed can affect the signaling pathway involved in breast cancer. Most of drugs were non-oncology drug repurposing type such as Pimozide, Aspirin, Metformin, Simvastatin, Niclosamide, Everolimus, Erlotinib, Amprenavir, Levofloxacin, Lamotrigine, Piperlongumine, Buformin, Tamoxifen, Pyrvinium pamoate and etc. Beside, most of the drugs repurposed significant inhibits proliferation, migration, and invasion by targeting PI3K-AKT pathway. Drug repurposed that can target Notch and TGF-β signaling pathway were less frequently introduced.

Conclusion: Breast cancer is associated by dysregulation of different signaling pathway. Our approach seems to offer promise for the identification the drug candidates that can inhibits aberrant signaling pathway in breast cancer. Our findings also showing that treatment with non-oncology drug repurposing is associated with lower risk mortality in breast cancer patients.

Keywords: Breast cancer, Drug repurposing, Drug repositioning, Signaling pathway

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Simple and Fast One-step PCR Method for Detection of a HOTAIR SNP (Research Paper)

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Introduction: HOTAIR, or HOX transcript antisense RNA, is an oncogenic long non-coding RNA (lncRNA), and multiple studies have demonstrated that HOTAIR is increased in a wide range of human malignancies. Single nucleotide polymorphisms (SNPs) are well known for directly regulating lncRNA expression and altering their activities. As a result, detecting single nucleotide polymorphisms (SNPs) is critical for understanding human diseases, identifying pathogenic variations, and implementing genetic modification programs. Here, we examine an easy and fast method to detect an SNP (rs17720428) related to the HOTAIR gene. Rs17720428 is one of the SNPs that increases the risk of gastric cancer.

Methods: Initially, 50 human DNA pools previously genotyped by Infinium HTS platform SNP array (Illumina Infinium GSA BeadChip—a robust, high quality assay) were examined using this approach. The primers were designed following Chen et al's strategy. The strategy makes use of the differential efficiency of genomic PCR using a primer that has a single mismatch with the chromosome that contains the SNP to be identified (usually the variant allele) against two mismatches with the corresponding alternative allele (often the wild type allele). The primer TM was set at 59°C. The cycling protocol was the same for all PCRs. Initial denaturation of genomic DNA took 5 minutes at 95 °C. This was followed by 35 repetitions of the steps: denature at 95 °C for 40 seconds, annealing at 59 °C for 40 seconds, and extension at 72 °C for 40 seconds. The last extension took 7 minutes at 72 °C. Before loading the PCR samples onto an agarose gel, no extra preparation was necessary.

Results: In this study, two PCR reactions were performed on each DNA sample, where one PCR reaction uses a primer with mismatches to detect the variant but not the wild type allele and the second PCR reaction employs a

primer with mismatches to detect the wild type allele but not the variant. The forward primer has two crucial characteristics. First, the primer's 3' nucleotide is at the SNP and pairs with the SNP residue to be identified. However, it is mismatched with the other allele residues. As a result, the nucleotides at the 3′ end of the variant and wild type primers differ. Second, two bases upstream of the SNP location, an additional alteration that is a mismatch with both the variant and wild type alleles was inserted to further differentiate the two alleles in PCR. In both cases, the reverse primer is the same. The variant primer has one mismatch relative to the variant allele, whereas the wild type primer contains two mismatches. As a result, the variant primer amplifies the variant allele preferentially. Likewise, the wild type primer identifies only the wild type allele. We successfully identified the wild type/mutant allele for lncRNA HOTAIR rs17720428 among 50 human DNA samples. The results were completely consistent with those from the SNP array.

Conclusion: In summary, this primer design method was evaluated on 50 human DNA samples. Result accuracy was 100%, as demonstrated by the SNP array. It thus indicates that this primer design strategy can be applied to known SNPs. It also saves time/effort and costs on reagents and makes SNP detection and genotyping by PCR substantially easier.

Keywords: SNP detection, PCR, one-step PCR, fast detection, Primer design

Simulation of a modern immunotoxin structure successful in breast cancer (Research Paper)

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Introduction: Breast cancer is the second-leading cause of cancer death and a major health risk for women. More than 40,000 deaths are expected in the United States in 2016, although recent advances in early detection have improved overall survival. The successful treatment of breast cancer in the last 10 to 15 years is one of the greatest achievements of medical science, especially in oncology, and is considered a medical revolution. Therefore, like other cancers, it is inevitable to deal with this type of disease to enable early diagnosis and effective treatment, where immunotoxins have a special place in targeted therapy. Immunotoxins have been used to treat cancer. The immunotoxin binds to the surface antigen of the cancer cell, enters the cell by endocytosis, and destroys the cancer cell

Methods: In addition, the recognition of specific antigens on the surface of cancer cells, the constituents of this type of drug and its composition based on peptide bonds, and the creation of recombinant proteins were among the requirements investigated in this bioinformatic, structural, and functional research. The properties of membrane antigens on the surface of breast cancer cells were evaluated using Docking, Modeller, and Gromacs software, as well as online protein structure prediction databases such as the Swiss Model and Protein Atlas

Results: The results of this research in the first stage led to the discovery of 10 antigens with the ability to bind to the surface of breast cancer cells with the highest and most specific expression of the EGFR antigen and, on the other hand, protein molecules that can bind. INS was selected as the most efficient ligand for this antigen. Next, the assembly of toxin from Pseudomonas with a selective ligand using the AAASGG 3 (GGGGS) linker in six modes resulted in six recombinant structures of different quality. The structures, among them the first structural model of the best protein in terms of structure and function, showed affinity and immunogenicity after exposure to realistic conditions. In general, the results of this research led to the introduction of the EGFR antigen as a suitable candidate for effective immunotoxins against the breast and the creation of an effective immunotoxin against this antigen with favorable structural and functional capabilities.

Conclusion: Hence, the targeted treatment of cancer through immunotoxin with the confirmation of the patent sequence led to the creation of a recombinant structure, which was analyzed with bioinformatics software. To ensure accurate results in the laboratory, we utilized Escherichia coli strain DH5 as a host during the cloning phase for plasmid DNA replication. This enabled a more precise and reliable replication process, thereby confirming the validity of our computational modeling, and the results of this research led to the modeling and simulation of the engineering structure of Cetuximab ZZpe38 immunotoxin. For future research, gene expression in mammalian cells will be the focus

Keywords: Breast cancer, toxin, ligand, EGFR antigen, immunotoxin drug

Sitagliptin enhances the cytotoxic activity of Cisplatin in a bladder cancer cell line HTB-9 (Research Paper)

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Introduction: According to recent research, there seems to be a link between cancer incidence and anti-diabetic drugs. Sitagliptin is a DPP-4 inhibitor that stimulates insulin secretion. Some research found a link between Sitagliptin use and pancreatic cancer progression. However, the impact of Sitagliptin on cancer development is debatable. Other studies have suggested that sitagliptin may have an inhibitory effect on the progression of cancer cells. To address this issue, we looked at the effect of Cisplatin and Sitagliptin combined therapy on the growth and viability of the bladder cancer cell line HTB-9.

Methods: The cells were grown in DMEM-HG medium with 10% FBS and 1% Pen/Strep at 37ºC. The IC50 values of sitagliptin and cisplatin were determined using the MTT test. HTB-9 cell lines were incubated with Sitagliptin and/or Cisplatin for 72h. Gene expression was studied using real-time PCR. Protein expression was examined through Western blot.

Results: Sitagliptin and cisplatin IC50 values were calculated to be 1545 and 4.2 g/ml, respectively. Treatment of HTB-9 cells with Sitagliptin or Cisplatin in

combination or alone resulted in a significant decrease in the expression of proliferation-dependent genes AKT, PI3K, and mTOR compared to the control group. In all treated groups, the noticeable increased expression of Bax was associated with significantly decreased Bcl2 expression. The algorithm for changing the expression of AKT, PI3K, and mTOR, Bax, and BCl2 was similar to that of their dependent genes. The expression of extrinsic and intrinsic apoptotic-related proteins (Caspase 8, Caspase 9, Caspase 3, and Caspase 7) increased significantly after Sitagliptin and/or Cisplatin administration. The group that received a combination of Sitagliptin and Cisplatin had the greatest effect on suppression of proliferation and induction of apoptosis.

Conclusion: Sitagliptin enhances Cisplatin's anti-cancer behaviour in HTB-9 cells by suppressing proliferation and increasing apoptosis.

Keywords: HT-B-9 cell line, sitagliptin, cisplatin, cytotoxicity

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Site-directed mutagenesis for the affinity improvement of the anti-PD-1 antibody by in silico modeling (Research Paper)

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Introduction: Cancer is a serious problem affecting the health of all human societies and the second leading cause of death worldwide. Monoclonal antibody-based immunotherapy is a type of targeted drug therapy for the treatment of cancer. Some monoclonal antibodies (mAbs) target immune checkpoint molecules for the treatment of several types of cancers. Programmable cell death 1 (PD-1) is an immune checkpoint protein that is expressed on activated T-cells, B cells, dendritic cells, natural killer cells, macrophages and monocytes. This protein plays a vital role in modulating immune responses. PD-1 ligand, PD-L1, is expressed on the surface of tumor cells to escape the antitumor immune response. Inhibition of the interaction between PD-1 and PD-L1 by mAbs has many therapeutic benefits and has led to a major advance in cancer treatment. Pembrolizumab is an anti-PD-1 mAb that was approved by the Food and Drug Administration (FDA) for 16 types of cancers. Complementary determining regions (CDRs) are regions in mAbs that bind to the antigen (Ag). The type of amino acids at the site of Ag and CDR interaction is important. Site-directed mutagenesis is one of the methods which is used to increase the affinity of mAbs. The conversion of neutral or negatively charged amino acids to positive amino acids in CDRs, especially CDR3, is one way to improve the affinity of mAbs. The purpose of this study was to optimize the affinity of the pembrolizumab using bioinformatics tools.

Methods: In this study, the structure of PD-1 in complex with pembrolizumab (wild-type anti-PD-1 Ab) was extracted from PDB server with 5ggs PDB code. SabDab server was applied to determine the sequences of CDRs. Then, PyMOL software was utilized for the investigation of interactions between anti-PD-1 Ab and PD-1 Ag. SWISS-MODEL server was used for modeling the three-dimensional structure of wild-type anti-PD-1 Ab, PD-1 Ag and mutated anti-PD-1 Abs. Moreover, we utilized the HADDOCK server and PyMOL software for the investigation of interactions between Abs and PD-1 Ag, and also for the identification of high-affinity mutated Abs.

Results: HADDOCK results showed that some of the mutations such as the replacement of arginine (R) with tyrosine (Y) at position 101 in CDR3 improved the binding affinity. The more negative HADDOCK score indicates the better affinity of the Ab. Moreover, the output files from the HADDOCK were investigated by PyMOL software. According to the results of the PyMOL software, the bonds length between Y101 in CDR3 and T76 in PD-1 Ag were changed by replacing R at position 101 (in R101, the number of bonds increased and the bonds length decreased).

Conclusion: mAbs have recently become one of the major methods for the treatment of cancer. Strategies for optimization of therapeutic mAbs can be applied to improve the affinity and function of mAbs. This study indicates that site-directed mutagenesis can improve the affinity of mAbs.

Keywords: Site-directed mutagenesis, Affinity, Pembrolizumab antibody, PD-1, Bioinformatics tools

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SLC11A1 gene expression changes and colon adenocarcinoma: An update of potential biomarkers and therapeutic applications (Research Paper)

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Introduction: Colon cancer is one of the most common cancers that occurs in men and women. Both environmental and genetic factors are involved in the occurrence of this cancer. Colon cancer usually occurs in people over the age of 50. Also, the presence of a history of colon cancer in one family can increase the probability of colon cancer in other family members. Environmental factors that increase the risk of colon cancer include obesity, high consumption of red meat, tobacco and alcohol. Based on studies, it is estimated that by 2030, new cases of colon cancer will exceed 2.2 million people and the number of deaths from this cancer will reach 1.1 million people. The most common type of colon cancer is colon adenocarcinoma (COAD), which occurs mainly in the intestinal mucosa. Colon adenocarcinoma usually grows in the intestinal duct and then spreads to nearby organs. This type of tumor is malignant and very aggressive and has a high mortality and recurrence rate. Despite the progress that has occurred in the treatment of colon cancer, including radiotherapy, chemotherapy, and surgical techniques, the prognosis of patients is still poor. Considering the role of different genes in various regulatory mechanisms such as DNA methylation, deacetylation of histones and also miRNA expression which can ultimately cause the occurrence and progression of colon cancer, there is little information about changes in SLC11A1 gene expression. And its role in the occurrence of colon adenocarcinoma is known. The aim of this study was to investigate changes in SLC11A1 gene expression in colon adenocarcinoma and introduce it as a diagnostic and prognostic biomarker.

Methods: TCGA data provided by Oncodb database was used to investigate SLC11A1 expression changes in colon adenocarcinoma. Also, based on TCGA clinical data, the relationship between the expression of this gene and the mortality rate of patients and clinical characteristics was appraised. Kaplan-Meier estimator was used to investigate the SLC11A1 gene expression changes and survival rate. Also, the biomarker status of SLC11A1 gene in relation to colon adenocarcinoma was evaluated using ROC diagram.

Results: The results of the investigations showed that the expression level of SLC11A1 in cancer samples increases significantly compared to normal samples (Log FC = 2.00, FDR < 0.001, p-value = 6.4e-23). Also, the results of this study showed that the expression level of SLC11A1 in the sample acquired from people whose BMI is more than 30 (Obese) compared to people whose BMI index is less than 30, significantly increases (p- value = 1.3e-10). In addition, the kaplan-meier estimator showed that increased expression of SLC11A1 is associated with poor prognosis of patients (LogRank p=0.03). Also, with the investigations carried out by the ROC diagram, it was found that the expression changes of the SLC11A1 gene can be considered as a good diagnostic biomarker for the diagnosis of colon adenocarcinoma (AUC = 0.88, p-value < 0.0001).

Conclusion: The results of our study showed that the expression level of SLC11A1 is increased in colon adenocarcinoma and is associated with poor prognosis of patients. As a result, it can probably play a role as an oncogene in the development of colon adenocarcinoma. It was also found that changes in the expression level of SLC11A1 in colon adenocarcinoma can be considered as a diagnostic and prognostic biomarker.

Keywords: colon cancer, colon adenocarcinoma, SLC11A1, Biomarker

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Specific Targeting of Recombinant Human Pancreatic Ribonuclease 1 using Gonadotropin-Releasing Hormone Targeting Peptide toward Gonadotropin-Releasing Hormone Receptor-Positive Cancer Cells (Research Paper)

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Introduction: Targeted drug delivery is a novel method to deliver anticancer therapeutics to tumor sites specifically. Gonadotropin-releasing hormone (GnRH) is a decapeptide, and its target-binding property has attracted attention as a means of targeted drug delivery. Human pancreatic ribonuclease 1 (hpRNase1) has been shown to exert anticancer properties when fused to a targeting moiety. The goal of the present study was to add a GnRH-targeting peptide to the N-terminus of hpRNase1 to target GnRH receptor (GnRH-R) expressing cells specifically.

Methods: The coding sequence of GnRH and hpRNase1 were fused, and the chimeric protein together with non-fused hpRNase1 was produced in E. coli (BL21). The recombinant proteins were purified, and their biological activity was evaluated using MTT and apoptosis assays. Non-parametric Kruskal–Wallis tests with Dunn's post hoc tests were performed to determine the significant differences between the study groups.

Results: GnRH-hpRNase1 chimeric protein specifically inhibited the proliferation of PC-3 (P=0.021), LNCaP (P=0.034), and AD-Gn (P=0.041) cells, while the growth of negative cells (AD- 293) was not significantly affected (P=0.081). GnRH-hpRNase1 decreased the IC50 values more than non-fused hpRNase1, by approximately 26.5-fold (P=0.036) for PC-3 cells, and exerted its growth inhibitory effects through apoptosis induction.

Conclusion: Fusion of GnRH to hpRNase1 structure produced an enzyme, which could specifically target tumor cells. This approach can be used to eliminate tumors, which harbor GnRH-R.

Keywords: Drug delivery systems, Ribonucleases, Pancreatic, Gonadotropin-releasing hormone

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Spiritual health center with hope for life in the elderly referring to Shiraz medical hospitals (Research Paper)

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Introduction: Aging is a gradual decay in the structure and organism of the body that occurs due to the intervention of the time factor. Spiritual health is one of the important aspects of human health, which provides a harmonious and integrated connection between internal forces. Hope is also a positive motivational state that is based on a sense of belonging and direction. Therefore, we decided to conduct a study with the aim of determining the relationship between spiritual health and life expectancy in elderly people referred to Shirazan Psychiatric Hospital.

Methods: This research is a descriptive-analytical study that was carried out cross-sectionally in 1400. The studied population consisted of 70 elderly people referred to Shiraz Psychiatric Hospital; who were included in the study in an easy and accessible way. Data were collected through demographic information, standard questionnaire of spiritual health and life expectancy. The SWBS spiritual health questionnaire contains 20 questions, including 10 questions in the field of existential health and 10 questions in the field of religious health, as well as the MHS life expectancy questionnaire, which contains 48 questions. The collected data were analyzed using descriptive statistics of mean, standard deviation and range of changes and inferential tests, onova, t test, Pearson's correlation coefficient in spss version 21 software.

Results: The participants in this study were 40 women (70%) and 30 men (30%). The average age of the elderly participants in this study 17.04 is ±1.67. The mean scores of spiritual health and life expectancy in the elderly under study are 71.4 ± 16.58 and 54.2 ± 63.93, respectively. There is a direct relationship between spiritual health and life expectancy, $P > 0.05$.

Conclusion: The results showed that the elderly have average spiritual health and average life expectancy. Also, there is a direct relationship between the spiritual health of the elderly and their life expectancy, and in other words, the elderly who have high spiritual health have a high life expectancy compared to others. Organization of workshops and meetings aimed at increasing the spiritual health of the elderly can have a great impact on the life expectancy of this group.

Keywords: Spiritual health, hope for life, elderly

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Stem cell therapy in stroke (Review)

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Introduction: Stroke is the leading cause of neurological disability in adults worldwide. It involves the significant impairment of sensory-motor function caused by cerebral ischemia and subsequent neuronal death and irreversible consequences. ascribed to a lack of medical or surgical treatments to improve neurological function and neurogenesis, chronic stroke places a massive burden on patients, their families, and society. Preclinical research over the past few decades has shown that in animal models of stroke, hematopoietic growth factors and stem cell administration or transplantation can improve recovery and functional outcomes in the post-ischemic brain. Stem cell therapy shows promise in reconstructing neuronal circuits and could be the next-generation therapy for stroke patients because it can prevent neuronal cell apoptosis, inhibit pro-inflammatory cell recruitment, secrete multiple neurotropic factors, and promote neural differentiation. In this review, we will provide a synopsis of different preclinical and clinical studies related to the use of stem cell-based stroke therapy

Methods: The papers included in this article were obtained from PubMed and MEDLINE databases. The following medical subject headings (MeSH) were used: “stem cell therapy”, “post-stroke neurogenesis”, “stem-cells stroke”, “stroke neurogenesis”, “stroke stem cells”, “stroke”, “cell therapy”, “neuroregeneration”, “neurogenesis”, “stem-cell human”, “cell therapy in humans”.

Results: Stem cell therapy has shown promising efficacy in the treatment of stroke, with various types of stem cells being studied, including granulocyte colony-stimulating factor, mesenchymal stem cells, autologous CD34+ peripheral blood stem cells, umbilical cord blood stem cells, and autologous adipose-derived mesenchymal stem cells. Furthermore, the administration or transplantation of hematopoietic growth factors and stem cells has demonstrated positive outcomes in terms of enhancing neurological function and neurogenesis in stroke patients. Among stem cell types, mesenchymal stem cells (MSCs) are currently the most extensively utilized for stroke therapy and have shown advantages in reducing apoptosis, neuro-inflammation, and enhancing angiogenesis in animal models of stroke. Human umbilical cord matrix MSCs (HUCMSCs) have also displayed potential

to promote tissue repair, functional angiogenesis, and neuroplasticity in animal models of stroke. Additionally, the use of granulocyte colony-stimulating factor (GCSF) has demonstrated efficacy in improving neurological function in patients with acute ischemic stroke; however, the degree of improvement may vary among individuals. Notably, a randomized controlled trial demonstrated the efficacy of GCSF treatment for acute ischemic stroke patients by yielding significant improvements in neurological function. Nevertheless, there are still concerns about administering stem cells directly into the brain through the intra-arterial route due to the potential for cell clumping and microthrombi formation. Consequently, some studies have found that intracerebroventricular administration of adipose-derived stem cells (ADSC) was more efficacious for neurological recovery compared to intravenous administration; nevertheless, this method also presents its own challenges.

Conclusion: Stroke is the leading global cause of adult neurological disability, which causes sensory-motor function impairment and neuronal death; however, there are currently no medical or surgical treatments to improve neurological function and neurogenesis in chronic stroke. Growing translational and clinical evidence has demonstrated the potential effectiveness of hematopoietic growth factors and stem cell transplantation as therapies for stroke.

Keywords: Stem cells, stroke, neural stem cells, mesenchymal stem cells

STEM CELLS UNDERGONE LOW IONIZING RADIATION IMPROVE MILD TRAUMATIC BRAIN INJURY (Review)

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Introduction: Stem cell therapy used in many branch of medicine and drug industry and regenerative medicine. X-ray and high level of radiation induces apoptosis, Reactive Oxygen Species (ROS) production, and genotoxic stress like Double-strand breaks (DSBs) in Deoxyribonucleic (DNA).

Methods: Although, Low Ionizing Radiation (IR; about less than 1 Gray) increased the differentiation of stem cells repair DSBs in DNA. In addition, low level radiation to Adipose Mesenchymal Stem Cells (ADSCs) increased Stat3 expression and decreased g-H2AX and Rad51 at 24 hours after radiation.

Results: Low Traumatic brain injury (TBI) resulting from damage brain cells temporarily, blow to the head or body in accident or shut gun wound. Also, the symptoms including, headache, nausea, fatigue, blurred vision, dizziness, and speech problems. Due to tissue sensitivity against radiation even low dose, especially the blood system and hematopoietic stem cells, it has become a European research priority network.

Conclusion: Furthermore, low dose radiation especially in gut and brain increased ROS, Superoxide dismutase 2 (SOD2), and activation of Nuclear factor kappa-light chain- enhancer of activated B cells (NFk). On the other hand, injection of stem cells into the cerebrospinal fluid (CSF) significantly decrease the number of hippocampus dark neurons, enhanced synaptic plasticity, improved the spatial memory, and decreased apoptosis in the CA1 region hippocampus. Stem cell have multipotent capacity to differentiation

cells and migrated into host cells. The long term therapy of stem cell could effective in mild brain injury.

Keywords: Traumatic brain injury, Stem cell, radiation, cerebrospinal fluid

Structural Properties of Human Chorionic Gonadotropin (hCG) Affected by Ultrasonic Irradiation: An in Vitro Study (Research Paper)

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1.

Introduction: Ultrasound, a mechanical energy form, is acoustic radiation at frequencies beyond the human hearing limit and can be transmitted into the human body. The impact of ultrasound is associated with heating, turbulence, shear stresses, dynamic agitation, and cavitation. The ultrasound application, at frequencies between 20 and 1 GHz, causes physical and chemical variations in a viscous medium through the collapse of cavities and cyclic generation [1-3]. Inevitably, the ultrasonic radiation interaction with living material disturbs the structure and features of biomolecules in a way that generally depends on the power and duration of exposure. The impacts of ultrasound can be divided into non-thermal and thermal mechanisms. However, the nonthermal biological impacts of ultrasonic radiation have still puzzled researchers. Despite several applications of ultrasound in the food industry [4,5], medical field [6], and pharmaceutical field [7,8], the details of ultrasound-induced disruption in protein structure remain unidentified. Several investigations on soluble proteins, such as whey protein [9], bovine serum albumin (BSA) [10], and integral membrane protein [3], have been performed. In all cases, sonication could denature proteins, and proteins' secondary and tertiary structures were altered. On the other hand, numerous recent investigates have shown that the public is unknowingly subjected to very high-frequency sound (11.2-17.8 kHz) and ultrasound (>17.8 kHz) signals in the air in public places [11]. Recently, there has been an increment in the number of systems that operate in very high frequency/ultrasound signals in public spaces. Hence, ultrasonic pollution is one of the important problems in the world and lots of people are at risk of being affected by ultrasonic pollution. There is sufficient evidence that noise can induce ischemic heart disease, sleep disturbance, and hearing impairment [12]. Recently, Daiber et al. demonstrated that environmental noise can induce oxidative stress and cardiovascular disease [13]. Noise exposure can increase the production of free radicals and the levels of malondialdehyde and catalase [14]. Noise pollution can also alter the DNA structure [15]. More importantly, a high level of noise pollution can act as a common source of stress on pregnant women making a diversity of psychological and physiological variations [12]. Bendokiene et al. demonstrated an association betweennhypertension amongst reproductive-aged women and the residential road traffic noise [16]. Human chorionic gonadotropin (hCG) is a peptide hormone and the most

acidic protein in humans that belongs to the gonadotropin hormone family [17]. This heterodimer protein has 237 amino acids (Fig. 1). Some of the variants of this placental hormone are highly sialylated glycoproteins [18,19]. hCG has the longest circulating half-life in human blood (about 36 h). This glycoprotein consists of two noncovalently joined subunits (α and β) [20]. The α-subunit has 92 residues, and the β-subunit includes 145 residues. The α-subunit is N-glycosylated at Asn52 and Asn78 and the β-subunit is N-glycosylated at Asn52 and Asn78. Previous studies have established that there are multiple variants of this hormone in urine and blood: free hCG, beta core fragment (hCGβcf), nicked hCG (hCGn), β-subunit (hCGβ) and nicked beta subunit (hCGβn) [21]. hCG has an extremely wide range of biological functions. This peptide hormone displays an essential role in maintaining pregnancy by adjusting the level of progesterone and estrogen. Additionally, during pregnancy hCG plays a key role in fetal growth and improves the anti-macrophage inhibitory factor. hCG detection is also effective in trophoblastic disease evaluation [22]. More interestingly, the hCG receptors are detected in the hypothalamus and hippocampus of the mother [23]. This glycoprotein hormone regulates local immune cell numbers and forces them to adopt a distinctive phenotype to protect and maintain the fetus [24]. Although there have been lots of efforts to identify the effects of ultrasonic irradiation on human health, there are few efforts carried out to identify the physicochemical mechanism of ultrasonic on protein structure. It should be also noted that in previous studies, the impacts of noise stress and noise pollution on the plasma level of gonadotropin hormones have been studied experimentally in vivo. However, there are a few reports about the impacts of ultrasonic on hCG structure in vitro from a physicochemical point of view. Furthermore, as mention earlier, the details of ultrasound-induced disruption in protein structure remain unidentified. As a result, due to the vital function of hCG, the objective of this study is to examine the possible effects of simulated ultrasonic irradiation (40 kHz) in various times of exposure (from 10 to 60 min) on hCG structure. This study is useful to achieve a better understanding of the physicochemical effects of ultrasonic irradiation on peptides and protein structures as an important class of bio-macromolecules. Besides, the findings obtained from this investigation can help to discover safe limits for people, particularly for pregnant women.

Methods: Materials: Highly purified hCG (5000 I.U., white, pyrogen-free powder, freeze-dried, and sterile) obtained from the urine of pregnant women, were acquired from Karma Pharmatech GmbH (Germany). ANS (8-anilino-1-naphthalene sulfonic acid), Coomassie brilliant blue, sodium dodecyl sulfate (SDS), 2-mercaptoethanol, NaH_2PO_4 and Na_2HPO_4 were purchased from Sigma-Aldrich Chemical Co. (USA) and CinnaGen Co. (Iran), respectively.

Deionized doubledistilled water (with the resistance of 18.3 MΩ) was consumed through all measurements. Experiments were obtained in phosphate buffer (PB) pH 7.4 (0.1 M). Instruments: The thermo scientific barnstead NANO pure water purification system (USA), the varian cary 100 bio UV-Vis spectrophotometer (USA), the AVIV 215 circular dichroism spectrometer (USA), the agilent cary eclipse fluorescence spectrophotometer (USA), the dynamic light scattering (DLS), Brookhaven Instruments Corporation, Holtsville (USA) and the Malvern Zetasizer Nano ZS (UK) were applied. The ultrasonic trials were performed in the WiseClean, digital ultrasonic cleaner-set WUC-D10H (South Korea) with a high frequency of 40 kHz and power consumption of 665 W. Sample Preparation: 25 μM hCG in PB (pH 7.4, 0.1 M) was put into small shielded tubes 1 cm × 1 cm (width and height). All tubes were filled with hCG solution, checking that no air bubbles remained in the tubes. The samples were divided into two groups: the control (reference) group as well as the experimental group. The control group (25 μM hCG in PB) was kept in small tubes and placed outside the ultrasonic apparatus and did not receive any treatment. The experimental group (25 μM hCG in PB) was placed in the ultrasonic apparatus. The ultrasonic irradiation time was altered from 10 to 60 min at 10 min intervals using a 40 kHz. UV-Vis (Ultraviolet-Visible) Absorption Measurements: The UV-Vis absorption spectra of the untreated and the experimental groups were scanned at a wavelength between 200-450 nm. In the beginning, the system was baselined with buffer solutions, and afterward, spectra of hCG solution (8 μM) were recorded. At first, the UV-Vis spectroscopic data of the control group were explored. Subsequently, the spectroscopic properties of hCG in the ultrasonic condition were scanned. To keep the temperature at 37 ºC, each measurement was achieved in a thermostated conventional quartz cell. Intrinsic and Extrinsic Fluorescence Measurements: The fluorescence of tyrosine residues of reference hCG (the control group) was examined. Subsequently, the emission properties of hCG immediately after 10 to 60 min treatment in the ultrasonic irradiation (the experimental group) were studied in the wavelength range between 293 and 360 nm via an excitation wavelength of 275 nm. Afterward, the accessibility of hydrophobic domains of the reference and the experimental group was determined by ANS fluorescence study in the wavelength range between 400-600 nm via an excitation wavelength of 350 nm. Samples including 30 μM ANS and 8 μM hCG in 0.1 M PB (pH 7.4) were prepared. To keep the temperature at 37 ºC, Protherms bath model NTB-211 temperature controller was utilized and a cuvette with a 1 cm path length, a 10 nm excitation slit, and a 10 nm emission slit was applied in each measurement. Circular Dichroism (CD) Measurements: The near-UV CD and far-UV CD spectra of the reference and the experimental groups at 37 ºC were recorded from 250 to 305 nm and 200 to 250 nm, respectively. Far-UV

CD spectra were scanned in a quartz cell (0.1 cm path length) with a 20 nm min-1 scan speed and a 0.2 nm resolution, on the other hand; near -UV CD spectra were taken with a 1 cm path length quartz cell. The concentration of hCG in the experiments for the far-UV region was 8 μM in PB and the concentration of protein in the experiments for the near-UV region was 25 μM in PB. Via subtracting the proper baseline, each of the CD spectra was corrected. The CD spectra deconvolution software (CDNN, version 2.1) was applied to deconvolute all CDspectra. Dynamic Light Scattering (DLS) and Zeta Potential Measurements: The hydrodynamic diameter of the control and the experimental groups were acquired at 633 nm and a fixed 90º scattering angle. Before measuring, all samples were filtered via nylon filters (0.20 μm). The zeta potentials of the reference and the experimental groups (8 μM hCG in PB) were also achieved. With the data from 5 runs, the average values of hydrodynamic diameter and zeta potential were determined. Gel Electrophoresis: SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) was performed to evaluate the effect of ultrasonic on hCG. The assay was performed consistent with the standard protocol [25]. The stacking (4% acrylamide, pH 6.8) and separating (12% acrylamide, pH 8.8) gels were run at a constant voltage of 100 V. The chambers of electrophoresis contain SDS (0.1%) and Trisglycine buffer (pH 8.3). The hCG solutions were diluted with a buffer containing bromophenol blue (1%), 25% Tris-HCl (pH 6.8, 1 M), SDS (2%), and glycerol (25%) and then heated at 95 °C for 5 min. The gels were stained with Coomassie blue (0.25%) dissolved in glacial acetic acid (10%), water, and methanol (45%) solution. The detaining solution contained water, methanol, and glacial acetic acid (8:1:1).

Results: UV-Visible Absorption Studies: To provide evidence for the structural effects of ultrasonic irradiation on hCG, UV-Vis spectroscopy measurements (one of the most constructive accessories for exploring the structural variation of bio-macromolecules) were carried out. The UV-Vis absorption spectra of hCG with and without ultrasonic irradiation are demonstrated in Fig. 2A. As revealed in this figure, this glycoprotein hormone has two main maximum absorption peaks (λmax): one at 214 nm region related to the n→π* transition of C=O (which is referred to peptide linkage) and at 276 nm region caused by transitions of π→π* of the aromatic residues [26,27]. After exposing hCG to ultrasonic irradiation, alterations in λmax at 276 nm region took place. As displayed in this figure, after 10 to 40 min of ultrasonic irradiation, it made an increment in the maximum absorption at 276 nm. These enhancements in λmax are indeed due to the disorders at the microenvironment of hCG [28]. Additionally, the absorption spectra showed that more side chains of aromatic residues of hCG were exposed to the solvent (inset of Fig. 2A) [20]. Our observation correlates with the results

presented by Vera et al. who showed that quinoa proteins subjected to ultrasound treatment had a noteworthy alteration in λmax and this result may point out a higher aromatic residue exposure and a greater degree of unfolding [29]. This data also correlates with those presented by He et al. who showed that as the ultrasonic irradiation time increases, the λmax of bovine serum albumin (BSA) increases obviously [30]. It should be noted that no obvious alterations in λmax at 214 nm after 10 to 40 min exposing hCG to ultrasonic irradiation were detected. However, after 50 min of ultrasonic irradiation, it made a reduction in the λmax at 214 nm but still made an increment in the λmax at 276 nm. This phenomenon could be assigned to a perturbation of α-helix induced via ultrasonic irradiation [31]. More importantly, the absorption spectra revealed that 60 min exposure to ultrasonic irradiation has an extremely high effect on the hCG structure and the λmax was vanished completely. Subsequently, ultrasonic irradiation can cause time-response changes in the tertiary structure of hCG. Generally, the biophysical effects of ultrasonic irradiation can be divided into non-thermal and thermal mechanisms. As a general rule, the bio macromolecules cannot absorb the acoustic energy directly, so this kind of energy affects bio-macromolecules indirectly by the non-thermal mechanism known as the cavitation phenomenon. This phenomenon increases free radicals in solution [30]. Accordingly, due to the cavitation effect, water molecules can produce some free radicals in solution which can initiate changes in the tertiary structure of hCG. It should be noted that the UV-Vis spectrum of hCG immediately after exposure to ultrasonic irradiation was not considerably different from hCG sample 1 h after 40-, 50- and 60-min exposure (Fig. 2B). Therefore, the time difference in assaying did not account for the variations detected. Hence, the ultrasonic-induced conformational modifications were irreversible. Steady-state Fluorescence Emission Studies: Fluorescence spectroscopy is one of the most powerful electromagnetic spectroscopies to examine protein folding and dynamics. There are three intrinsic fluorophores for almost all proteins: Tyr (tyrosine), Trp (tryptophan) and Phe (phenylalanine). However, hCG contains 7 Tyr residues and does not have any Trp residues [32]. Thus, fluorescence spectra of Tyr residues in hCG were applied to discover hCG conformational variations under ultrasonic irradiation. It should be mentioned that the application of Phe or Tyr fluorescence emission is limited to tryptophan-free protein [33]. Tyr residue is regarded as a simple fluorophore and seems to be relatively insensitive to the protein local environment. However, if there are no proton acceptors in the local environment of protein and the phenol side chain is shielded from a solvent, intermolecular and intramolecular interactions can reduce the quantum yield of Tyr [34]. It has been also published that the phenol hydroxyl group ionization causes the fluorescence quantum yield reduction. Tyr fluorescence emission in hCG has

a maximum intensity (λmax,em) around 303 nm [34]. Figure 3A displays fluorescence spectra of hCG with and without ultrasonic irradiation at 37 ºC. As displayed in this figure, after 10 min of ultrasonic irradiation, it made a very slight reduction in the fluorescence emission of Tyr residues (~2%) with no shift. However, 20 min treatment in the ultrasonic irradiation had a greater influence on hCG than 10 min exposure to ultrasonic irradiation (~48%) and longer periods (>20 min) made the fluorescence vanish completely. Consequently, according to our data, the ultrasonic-induced alterations were identified in the intrinsic fluorescence emission of Tyr residues in hCG. Such a manner suggests that ultrasonic condition induced variation in fluorescence emission of Tyr residues via varying the position or structure of Tyr residues of hCG [20]. Similarly, He et al. and Jiang et al. indicated that the λmax,em of BSA [30] and black bean protein [35] reduce noticeably compared with those samples without ultrasonic irradiation. As mentioned earlier, hCG is a tryptophan-free glycoprotein, therefore any reduction in the fluorescence emission of this protein is owing mostly to Tyr and Phe residues. Consequently, based on our results and previous results [30,35] we can propose that the cavitation effect of ultrasonic irradiation can induce the aromatic residues oxidation, therefore, can cause hCG unfolding. The hydrophobic fluorescent probes can be consumed to recognize the protein surface hydrophobicity. It is well accepted that the hydrophobic interactions are very crucial for conserving the conformation, stability, as well as function of proteins [9]. ANS, as an organic substance, is generally utilized for discovering the tertiary/quaternary structure of protein molecules because ANS fluorescent only after associated with the hydrophobic surface of protein [36]. Figure 3B revealed that the surface hydrophobicity of hCG is low. After 10 min treatment with ultrasonic irradiation, very low ANS affinity was observed for hCG, too. However, after longer periods (>20 min) treatment with ultrasonic irradiation, ANS affinity to hCG increased considerably. This data revealed the hydrophobic core formation in the hCG after treatment with ultrasonic irradiation. The alteration in hydrophobicity as a function of ultrasonic irradiation time are extremely noteworthy, presumably because of the unfolding of hCG. Nevertheless, as shown in Fig. 3B, the surface hydrophobicity reduced after sonication for 60 min, which is a symbol of protein aggregation. This result is in consistent with the data from increasing surface hydrophobicity of whey protein concentrate for up to 5 min of sonication and decreasing its surface hydrophobicity for more than 5 min [9]. It has been published that the exposure of hydrophobic groups can lead to the change in the tertiary structure of proteins [37] which is in good agreement with UV absorption data as mentioned above. As mention earlier, the cavitation phenomenon can affect water molecules and produce some free radicals in solution. It is widely accepted that water molecules play a key role in the folding and self-assembly of proteins [38]. As a result, it could be

hypothesized from our observations and previous results [30,35] that ultrasonic irradiation can change the structure of water molecules, consequently, the structure of hCG modifies. However, it should be emphasized that further experiments must be done to conclude the underlying mechanisms. In consequence, the obtained extrinsic and intrinsic fluorescence data specified that ultrasonic irradiation initiates structural changes in hCG.CD Studies: CD spectroscopy can measure any alternation in the secondary/tertiary structure of macromolecules, typically proteins [39]. With the purpose of considering the impact of ultrasonic irradiation on the hCG structure, the far-UV CD method was employed, and the CD spectra are shown in Fig. 4A. As displayed, the far-UV CD spectrum of hCG was detected via the presence of a remarkable negative band at around 208 nm wavelength. Our observations are coincident with those published by Fralish et al. [40]. Compared with the control sample, far-UV CD studies of hCG subjected to ultrasonic displayed significant changes in its secondary structure particularly after 60 min (Fig. 4A). Subsequently, the content of the hCG secondary structure was calculated. hCG consists of 11.97% α-helix, 35.01% β-sheet and 16.48% β-turn (Table 1). Accordingly, hCG is primarily a β-structure protein [40]. Ultrasonic irradiation after 10 min made an insignificant change in the secondary structure content of hCG, conversely, longer periods (>20 min) made an obvious alternation in the secondary structure content of hCG. Consequently, as the ultrasonic exposure time increased, the α-helix content reduced and the content of the β-sheet barely altered, and at the same time, the content of the random coil structure increased. Obviously, after 60 min exposure, the secondary structure of hCG was changed clearly and a transition to the random coil appeared. Interestingly, our data correlate with those of Li et al. [37] who have shown that ultrasonic irradiation at high power condition (>600 W) can increase a transition from α-helix to the random coil in the secondary structure of alcalase hydrolysates. The protein secondary structure depends on the interactions between various parts of the protein along with the local sequence of amino acids, thus it is probable that ultrasonic irradiation disrupts these interactions. The previous study also displayed that the decrease in α-helix content of protein might be owing to the hydrophobic surface exposure [37]. Hence, ultrasound irradiation could initiate the interactions breakdown that stabilizes the structure of hCG, for example, electrostatic interactions and/or hydrogen bonds. This phenomenon can lead to the protein unfolding [29], and the hydrophobic patches could be exposed to the surface of hCG. This conclusion is consistent with our observation from the ANS fluorescence studies. It should be mentioned that the far-UV CD spectrum of hCG immediately after exposure to ultrasonic irradiation was not considerably different from hCG sample 1 h after 40-, 50- and 60-min exposure (inset of Fig. 4A). Therefore, the time difference in assaying did not account for the

variations detected. Near-UV CD is an appropriate technique to observe any variations in proteins' tertiary structure. The near-UV CD spectrum of protein depends not only on the microenvironment of the aromatic amino acids side chain (related to the π→π* transition) but also on the disulfide bonds (related to the n→σ* transition) and even the non-protein cofactors [39]. hCG, As reported contains 6 Phe residues, 7 Tyr residues, and 11 disulfide bonds [32]. The CD spectra of hCG with and without ultrasonic irradiation are demonstrated in Fig. 4B. There are two notable minima at 262 nm and 268 nm in the hCG near-UV CD spectrum which are attributed to Phe residues [39]. After 20 min of ultrasonic irradiation, it made a reduction in this remarkable minimum. Also, 30 min treatment in the ultrasonic irradiation had a greater impact on this peak. Besides, for longer periods (>30 min), fine structure and loss of CD signal took place at this wavelength. The near-UV CD spectrum of hCG also showed a remarkable minimum between 275-285 nm, which is attributable to the phenolic group of Tyr residues. It should be mentioned that the near- UV CD spectrum of disulfide bonds arises around 260 nm wavelength and is mostly quite weak. After exposing hCG to ultrasonic irradiation (>30 min), the amount of the peak at this region reduced. Indeed, the reduction in the asymmetry of the hCG tertiary structure caused these variations. This observation reveals good agreement with UV-Vis absorption as well as fluorescence emission data as mentioned above .Dynamic Light Scattering (DLS) and Zeta Potential Studies: DLS is the greatest technique for monitoring the biomacromolecules size. Accordingly, the DLS technique was exploited to find out the effects of ultrasonic irradiation on hCG size distribution. As demonstrated (Fig. 5), the peak diameter of native hCG is 4.1 nm. The effect of ultrasonic time revealed initial increment and eventual reduction in peak particle size. These alterations indicated that ultrasound in an aqueous system could promote interactions of hCG molecules and making some larger particles. Arzeni et al. [41] and Gülseren et al. [10] established that highintensity ultrasonic irradiation increased the size of particles in egg white protein and BSA. Nevertheless, after 60 min treatment in ultrasonic irradiation, the peak diameter reduced. Ultrasonic processing for this long time possibly induced some larger particles dissociated into smaller ones. Ultrasound-caused protein dissociation has been reported earlier. The germin-like protein was reported to dissociate into smaller size after 40 min ultrasonic treatment [42]. It has been reported that at the air-liquid interface of ultrasonic-induced bubbles, proteins could be destabilized, causing the protein particles aggregation and homogenization [42]. Consequently, it could be concluded that the sensitive balance between various noncovalent interactions in the structure of hCG can be easily disrupted via ultrasonic irradiation, causing protein denaturation.Moreover, hCG aggregates formed by the non-covalent interactions could be removed with excessive ultrasonic duration, causing hCG particle breakage. A physical

term, zeta (ζ) potential value, is the most significant reference about the surface charge of biomacromolecules [39]. The protein surface charge is dependent to the protein environment. The ζ-potential of hCG with and without ultrasonic irradiation are listed in Table 2. The ζ -potential of hCG was found to be around -16.42 mV. hCG is the most acidic glycoproteins with an isoelectric point (pI) value ranging from 3-7 and has almost 15 sialic acid residues per molecule [18], which was responsible for the obtained negative ζ-potential. Table 2 elucidates that ultrasonic irradiation caused a notable ζ-potential enhancement in hCG, besides, the ζ-potential variation between the hCG with and without ultrasonic irradiation became greater at longer ultra-sonication times. Consequently, hCG structural fluctuation is in combination with the surface charge alteration. As a result, ultrasonic irradiation can increment the extent of charged residues existing at the hCG surface. This result is consistent with a remarkable alteration in ANS access to the hCG hydrophobic sites; i.e., ultrasonic irradiation prompted hCG structure alterations. Our results are coincident with those presented by Gulseren et al. [10] and Jiang et al. [35] who showed that the ζ-potential and surface hydrophobicity of patches of ultra-sonicated BSA and black-bean protein isolate enhanced compared to the native form of protein samples. This result could be associated with the fluctuation of water contents around hCG microenvironments. Consequently, ultrasonic irradiation could increase the negative surface charge on hCG and strengthen the interparticle electrostatic repulsions. Gel Electrophoresis Analysis: Electrophoretic protein patterns obtained through SDSPAGE for ultrasound treated and untreated hCG are revealed in Fig. 6. As revealed in this figure, hCG presented two major bands representing the α subunit and the β subunit. hCG is a glycoprotein with multiple glycosylation sites, including four in the β-chain (MW 22.2) and two in the α-chain (MW 14.5 kDa), thus, the subunits do not run exactly on SDS-PAGE. This result was in accordance with the reports by Pong et al. [43]. No difference in the hCG fractions was distinguished between untreated and sonicated hCG after 40 and 50 min. The obtained results are in agreement with previous literature [44]. However, after 60 min treatment in ultrasonic irradiation, some new bands were observed. The appearance of these new bands might be due to protein hydrolysate. The results displayed that considerable fluctuations occurred to the hCG structure upon treatment with ultrasound after 60 min. This pheromone has been reported by other groups [45,46].

Conclusion: Nowadays, there are some pieces of evidence that ultrasound can alter the function of cells and their components such as proteins and enzymes. Although some previous studies disclosed that ultrasound can alter the physical, chemical, and biological properties of proteins, behind these

works, there are some investigations exhibited that ultrasound had no significant effects on proteins [9]. Due to the vital action of hCG, investigating the effects of ultrasound on hCG are essential for discovering safe limits for people particularly for pregnant women. In this study, the UV-Vis studies and near-UV CD results verified that ultrasound (>30 min) can generate alternations in hCG structure. Additionally, the ultrasonic-induced conformational variations were irreversible. Besides, the ultrasonic-induced deviations were recognized in the intrinsic fluorescence emission of Tyr residues in hCG. Additionally, the alterations in hydrophobicity as a function of ultrasonic irradiation time are noteworthy. Our far-UV CD data demonstrated that as the ultrasonic exposure time increased, the α-helix content reduced, and the β-sheet content barely changed, and the random coil content structure increased. The DLS and ζ-potential surveys showed that ultrasonic (up to 50 min) can cause size and surface charge enhancement in hCG. Nevertheless, after 60 min treatment in ultrasonic irradiation, the peak diameter reduced. In the SDS-PAGE experiment, no difference in the hCG fractions was distinguished between untreated and sonicated hCG after 40 and 50 min. However, after 60 min treatment in ultrasonic irradiation, some new bands were observed. Consequently, our results, i.e., significant loss of tertiary structure, higher ANS binding to the hydrophobic patches, and increment of the random coil content, suggest that hCG after exposure to ultrasonic radiation is unfolded. It would be possible that the sensitive balance between various noncovalent interactions in the structure of hCG can be easily disrupted via ultrasonic irradiation. Furthermore, after 60 min treatment in ultrasonic irradiation, hCG was hydrolyzed. Our in vitro experiments showed ultrasonic treatments of hCG resulted in time-dependent structural variations. However, the question of why some proteins were altered by ultrasound and some were not is still open.

Keywords: Human chorionic gonadotropin , Tryptophan-free protein, Ultrasonic irradiation, β-Structure profile

Structure and function of papain proteinase enzyme (Review)

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Introduction: Carica papaya or tree melon is a plant native to the tropical regions of America. Papain proteinase is an enzyme that is extracted from the juice of unripe papaya fruit. This enzyme has proteolytic function with cysteine protease activity from endolytic plant. Papain is obtained by collecting papaya juice. After this juice is dried, it is purified in order to purify it. Papain is widely used in hydrolysis of short chain peptides, proteins, esterified amino acid and amide bonds, drug production and food proteolysis. This enzyme has been discussed both biologically and industrially, papain. This enzyme has proteolytic function with cysteine protease activity and is obtained from unripe green papaya juice. Papain grows in all tropical regions and in all seasons; Because it is resistant in a wide range of Ph and temperature. This enzyme breaks down organic molecules made of amino acids, known as polypeptides. This enzyme is used in industries: food, pharmaceutical, leather, meat, detergents, etc. Structure: Papain proteinase is a single-chain protein. Protein folding and conformation is influenced by the hydrophobicity of papain with the outer hydrophilic core interacting with water and stabilizing the inner hydrophobic core in the tertiary structure. The protein is stabilized by three internal disulfide bridges that bring the molecule together along these bridges, creating a strong interaction between the side chains that contributes to the stability of the enzyme. The papain molecule has a second fully alpha sheet and a second antiparallel beta sheet. Hydrophobic interactions have the greatest effect on protein structure and hydrophobic amino acid side chains. In general, it can be said that the enzyme is more stable in hydrophobic solvents. Function: This enzyme specifically binds to peptides containing positively charged amino acids, mainly lysine, arginine, and phenylalanine residues. Papain proteinase converts proteins into polypeptides and dipeptides. In the active site of this enzyme, there are three amino acids Cys, His and Asp. This enzyme attacks inside the peptide chain that has a free N-terminal. The mechanism by which it cleaves peptide bonds involves deprotonation of Cys25 by His159. Asp175 helps to orient the imidazole ring of His-159 to enable this deprotonation. Although these three amino acids are far apart in the chain, they are close together due to their folded structure. Application: Proteinases convert proteins into polypeptides and peptides. This feature is widely used in various industries. Among the uses of papain proteinase, we can mention: food industry, health care, pharmaceutical and

medicine, drug design, detergent and textile industry. One of the uses of papain is in pharmaceuticals and medicine. This fruit is rich in antioxidants. Among the effective properties of papaya fruit are increasing blood platelets, treating menstrual pains, activating growth hormones, regenerating muscle tissues, treating fungal infections, treating throat disorders, preventing arthritis, increasing heart health, treating wounds, relieving pain and anti-tumor effects.

Methods: Many studies have been done on the function of papain proteinase enzyme on the body. For example, during recent research it has been found that papain can improve athlete's foot fungal infections, or animal studies on wounds have shown that papain-containing ointments can improve wound healing and collagen deposition, and this enzyme can also help indigestion. Relieve patients sensitive to gluten, and in recent studies on cancer mice, it has been shown that papain injection is effective in the process of tumor healing.

Results: This review provides an overview of the structure and function of papain. Papain plays a vital role in pharmaceutical food, health care industry, detergents, cosmetics, textiles and leather. Papain is an inimitable enzyme class and has proteolytic activity with cysteine protease activity from endolytic plants. The source of this enzyme is green papaya juice.

Conclusion: Currently, papain is widely used in various industries because it covers the stages of the biocatalyst cycle. With the advancement of technology, it is now used to treat fatal diseases. In addition, they are investigating more benefits of papain so that it can be used in drug design. It can be hoped that this enzyme can be genetically and chemically modified by protein engineering and recombinant DNA, so that it can be used for ideal biotechnology and industrial applications.

Keywords: Papain proteinase, Carica papaya, structure, function, applications

studies of the binding ability of some pentamidine based compounds with B-DNA as anti-cancer agent by molecular docking (Research Paper)

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Introduction: The connection between nucleotides in the double-stranded helix of DNA is such that grooves are created on DNA. These grooves are divided into two major grooves and minor grooves. These grooves are the places where DNA is connected to proteins, chemicals, and drugs. Today, most anticancer drugs work by interacting with DNA. A group of anticancer compounds that bind to the minor groove of DNA through covalent and non-covalent bonds are called MGBs. Pentamidine is a drug that affects the nucleus of protozoan cells and by binding to mitochondrial DNA causes cell destruction and death. This compound is known as an anti-cancer agent. Today, cancer is one of the most important genetic diseases, which is accompanied by a change in the process of natural cell division and disruption. The aim of this research is to study the binding ability of pentamidine-based compounds with B-DNA as an anti-cancer agent using molecular docking

Methods: The connection between nucleotides in the double-stranded helix of DNA is such that grooves are created on DNA. These grooves are divided into two major grooves and minor grooves. These grooves are the places where DNA is connected to proteins, chemicals, and drugs. Today, most anticancer drugs work by interacting with DNA. A group of anticancer compounds that bind to the minor groove of DNA through covalent and non-covalent bonds are called MGBs. Pentamidine is a drug that affects the nucleus of protozoan cells and by binding to mitochondrial DNA causes cell destruction and death. This compound is known as an anti-cancer agent. Today, cancer is one of the most important genetic diseases, which is accompanied by a change in the process of natural cell division and disruption. The aim of this research is to study the binding ability of pentamidine-based compounds with B-DNA as an anti-cancer agent using molecular docking

Results: e.In this research, all pentamidine derivatives bind with B-DNA and the best result is related to the docking of compound number 2 Benzenecarboximidamide, 3,3'-(1,4-butanediylbis(oxy))bis- with the most negative binding energy level -8.11 and Also, compounds No. 1, 3, 4, 6, 7, 8, 10, 11, and 12 studied in this research showed more negative and better binding energy level than the standard compound.

Conclusion: According to the results of molecular docking of pentamidine derivatives in In Silico studies, these derivatives should be investigated in laboratory conditions for additional investigations.

Keywords: pentamidine,anti-cancer,molecular docking,B-DNA,Connectivity

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Study Allan-Herndon-Dudley Syndrome in a Iranian Family with novel SLC16A2 mutation: a case report (Research Paper)

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Introduction: A deficiency of monocarboxylate transporter 8 (MCT8), which is encoded by the SLC16A2 gene known as Allan-Herndon-Dudley syndrome (AHDS). Xq13.2 is where the SLC16A2 gene is found. The SLC16A2 gene is in charge of making it easier for thyroid hormone to cross the blood-brain barrier and enter cells, including active T3 and T4. A variety of variants, including missense, nonsense, insertion, deletion, and splicing variants, can result from mutations in the SLC16A2 gene. This neurodevelopmental condition is characterized by thyroid functioning abnormalities as well as delays in mental and motor development. In patients with AHDS, the degree of delayed myelination varies. This variation makes clinical diagnosis difficult and frequently results in underdiagnosis of the condition

Methods: whole-exome sequencing (WES) and data analysis On the patient's pripheral blood sample sample were carried out. The mutation was confirmed by Sanger sequencing in the patient , his mother and his brother

Results: We reported a six-year-old with AHDS diagnosis and pathogenic novel deletion mutation(c.467_469del/p.Phe156del) in the SLC16A2 gene manifesting normal levels T3,T4 and TSH. Additionally, three pathogenic variants have been reported in the proband in the genes TDP2, ALDOB and PMFBP1 as secondry finding. Common symptoms in both Proband and his brother include frequent vomiting in infancy, seizures, developmental delay

accompanied by speech difficulties, muscle atrophy and body hypotonia, clenched fists, sclerosis, and skull region depression in the Proband, as well as epilepsy. The MRI result for the Proband has been normal. The mother, who is a carrier of this mutation, had a small right ear and atrophy of the right ear canal was observed. Furthermore, she has experienced two miscarriages in the first and fourth pregnancies.

Conclusion: The study of the familial case afflicted with the Allan-Herndon-Dudley syndrome highlights challenges and complexities associated with diagnosing rare genetic disorders. Through the utilization of next-generation sequencing (NGS) technology, a powerful tool in the field of genetics, a definitive diagnosis was achieved for the affected individuals.We identified a novel mutations in the MCT8 (SLC16A2) gene in two son from a family with AHDS by Next Generation Sequencing. The tests related to the levels of T3,T4, and TSH have been normal, and no specific issue was observed in the MRI of the proband. This confirms the presence of a broad spectrum of symptoms in this disease, which has made the diagnosis itself challenging.

Keywords: Allan-Herndon-Dudley syndrome, whole-exome sequencing, SLC16A2

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Study of lncRNA BANCR expression in tumor tissues and adjacent normal tissues in Gastric cancer patients (Research Paper)

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Introduction: Long non-coding RNAs (lncRNAs) have emerged as crucial regulators in various biological processes, including cancer development and progression. This study aimed to investigate the expression differences of the BRAF-activated non-coding RNA (BANCR) gene in GC tissues compared to adjacent normal tissues. The potential diagnostic significance of BANCR in GC was explored, with the aim of improving diagnostic and therapeutic approaches for this global health burden.

Methods: Tissue samples from 100 gastric cancer (GC) patients were collected, and BANCR expression was analyzed using quantitative real-time PCR. Correlations between BANCR expression and clinicopathological features were assessed, and its biomarker potential was evaluated.

Results: In individuals diagnosed with GC, the expression of BANCR was notably elevated in tumor tissues compared to adjacent normal tissues ($P < 0.0001$). However, the analysis of gene expression data did not demonstrate any statistically significant correlation between elevated BANCR expression and clinicopathological features. According to the ROC analysis, BANCR demonstrated an AUC of 0.6733 ($P < 0.0001$), with a sensitivity of 73% and a specificity of 45%. However, further evaluation is required to determine its potential as a biomarker (CI 95% = 0.5992 to 0.7473).

Conclusion: The observed upregulation of BANCR in GC tissues implies its potential involvement as an oncogenic lncRNA in GC patients. Furthermore, BANCR may serve as a promising biomarker for identification and treatment of GC.

Keywords: BANCR, gastric cancer, H. pylori, LncRNA, RT-PCR, TNM

Studying on the importance exosomes pluripotent stem cell derived mesenchymal stromal cells (hipsc_MSCs) protect liver against hepatic ischemia (Review)

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Introduction: in recent years, the MSCs derived from human induced pluripotent stem cells (hipscs) has been used in pre-clinical studies and showed better performance compared to the adult MSCs in terms of cell proliferation, immunomodulation, cytokines profiles production of microenvironment modulating exosomes and secretion of bioactive paracrine factors. It has been shown that hipsc_MSCs can prevent I/R damage in the kidney, liver and heart. Recent studies have further reported that EVs secreted by ADMSCs can deliver mirs such as mir181_5p and mir122 to inhibit the development of HF.

Methods: we reviewed about 22 articles are conducted from 2019 to 2023 in the world and Iran. We searched some key words such as exosome, mesenchymal stem cell, extracellular vesicles, mir150_5p, liver fibrosis in ScienceDirect, Elsevier, PubMed and SID. we reviewed about 22 articles are conducted from 2019 to 2023 in the world and Iran. We searched some key words such as exosome, mesenchymal stem cell, extracellular vesicles, mir150_5p, liver fibrosis in ScienceDirect, Elsevier, PubMed and SID.

Results: the administration of MSCs as a therapy for liver disease holds great promise, it can differentiate into hepatocytes, reduce liver inflammation, promote hepatic regeneration and secrete protective cytokines. Several studies have shown that exosome derived from MSCs play a major role in promoting hepatocyte proliferation and maintaining hepatocyte function. It was also confirmed that either circDIDOL over expression or mir 141_3p inhibition suppressed LX2 cells proliferation, resulted in cell cycle arrest and induced cell apoptosis. Moreover, mir141_3p inhibition reduced the protein levels of α-smooth muscle actin (α_SMA) and type I collagen (colI) inLX2 cells by elevating PTEN to suppress the AKT pathway. There is a study demonstrating that mir181_5p, which was secreted by ADMSCs can reduce liver fibrosis by reducing transforming growth factor beta (TGFβ) induced HSCs activation due to directly suppressing STAT3, Bcl2, Beclin, pathway and increasing autophagy. In addition, du et al, isolated EVs from ADMSCs and cocultured

with HSCs, they found that ADMSCs derived EVs containing mir150_5p attenuate hepatic fibrosis by inhibiting cxcl1 expression. Cxcl1 is ligand for cxc chemokine receptor2, which has also been documented to be expressed in HSCs. Further experimental results indicated that circCDK3 mediated liver fibrosis by regulating the mir17_5p, KAT2b axis, and KAT2B can promoted MFGE8 transcription by H3 acetylation. Hence HbMSCs derived exo circCDK13 can inhibit liver fibrosis. More over recent studies have demonstrated that hbMSCs_EXs inhibited HSCs activation via the wnt/βcatenin pathway in vitro and in vivo. MSCs express antigen cluster of differentiation CD105, CD73 and CD90 but they lack CD45, CD34 and human leukocyte antigen HLA class Π. In a culture system that allowed MSCs to be in contact directly with HSCs the suppressed HSC proliferation by upregulating the notch1 expression and down regulating the p13k, AKT pathway, a critical pathway inducing HSC proliferation in HSCs, although the exact mechanism by which notch1 decreased p_AKT in HSCs has not been elucidated. It has also been reported that MSCs prevented HSCs from entering this phase by upregulating the inhibitors of cell proliferation such as p27kip, and p21cip1, and downregulating the accelerators of cell cycle namely, cyclinD and PERK. Phosphorylated ERK1/2 that is highly associated with HSC proliferation was also found to be reduced in HSCs cocultured with MSCs.

Conclusion: To summarize, the current study revealed that EVs derived from ADMSCs deliver mir150_5p to down regulated the expression of CXCL1, which inhibits the development of HF. Exosome could intracellularly activated the generation of sip and sk1 activity in the target hepatocytes. The results indicated that hbMSCs_EXs are responsible to induce the recovery of markers associated with improved liver function, inhibition of inflammation and increased hepatocyte regeneration.

Keywords: exosome, mesenchymal stem cell, extracellular vesicles, mir150_5p, liver fibrosis

Subliminal and revitalization of teeth (Research Paper)

zakiyeh khosravi,[1,*]

1. medical

Introduction: In recent decades, several studies have been conducted in the direction of isolating dental stem cells, while still the nature The mesenchyme of these cells has not been discussed and studied; the purpose of writing this article is to examine tooth reconstruction in old age different by using mesenchymal cells extracted from dental pulp and also studying the successful experiments conducted in this field Is. In the present study, the third molar teeth of adults aged between 25-18 were extracted for various reasons such as orthodontics, prophylactics, etc. were used.. the follicle and pulp of these teeth after being extracted and stored in the laboratory under certain conditions were cultured and after checking in the first and second passages, in the third passage, they were examined genetically with the help of flow cytometry. were placed. Also, this issue can be seen in the milk teeth of children between 6-11, which after collecting and placing in the laboratory environment The pulp and follicle of the teeth were separated from it and were cultured in the laboratory under special conditions and subjected to genetic analysis. gave According to the discoveries mentioned in the above article, it is necessary to mention that mesenchymal cells of teeth, including mesenchymal cells Third molar teeth are a very rich source of dental pulp cells, which after collecting, culturing and passaging them in the conditions It can be found that these cells are found in all people (adults, children and even fetuses) and the possibility of using this Cells are unlimited in any period.The hidden point is that in the use of these cells, these cells can be used in medical science because it is free from all harm. And predictable problems in implants and... are far away. Also, another potential advantage of these cells is their high adaptability Dealing with the immune system, which makes it easier to do this because these cells are equal to the immune systemAnd after planting, the possibility of being rejected by safety messages is very low, and this makes it use. Pulp of another tooth is doable for a person and far from danger.

Methods: 14 samples from the pulp and 6 samples from the third molar dental follicle of adults between 18 and 25 years old were collected. They were extracted due to malocclusion or orthodontic treatment with expert diagnosis and with the prior consent of the patients. These teeth are missing There were caries or previous restorations and all the patients were healthy and did not have any systemic diseases. Tooth samples after being pulled

into tubes containing 1640 RPMI, Gibco containing antibiotic x2(2 times the strength of Penny Cilin and streptomass yen, Gibco) were placed and transferred to the molecular cell laboratory at a temperature of 4 degrees Celsius and for Revealing the pulp chamber, the teeth were cut from the enamel-cement connection by a carbide disc and a handpiece. And after that, the pulp was separated from the teeth by means of a fine file; then to culture pulp and follicle tissue cells by No. 10 surgical blade, these cells were divided into smaller pieces, and then they were placed in a Falcon containing 4 mg/ml collagen T solution (I sigma, 104 mg/ml dispase type solution (Gibco) at a ratio of 1 1/ for 45 They were kept at 37 degrees Celsius for 10 minutes, and then they were added to the lysed tissue of the culture medium and incubated for 10 minutes with Around 600 grams were centrifuged. The resulting cell plate with a mixed culture medium and after transferring to a suitable zvt in an incubator with a temperature of 37 degrees Celsius and 5 atmospheres And 2% CO2 was cultivated This culture medium was changed every two days until 70% of the bottom of the plate was filled with cells, when the bottom of the plate was 70% filled. The samples were passaged with EDTA _trypsin. and finally from flow cytometry analysis to investigate the phenotypic profile of surface markers and the nature of stem cells from the tissueThe pulp and follicle of the third molar tooth were used for this purpose, the cells were placed in the third passage of trypsin and in the form of a suspension in one milliliter (saline buffer phosphate (PBS) with a concentration of 1,000,000) Then the cells were divided into 6 tubes and 5 µl of PE with antibody was added to each tube and the tubes were then kept at 4 degrees Centigrade for 30 minutes, they were placed in the dark environment, and after this period, the cells were washed with 1 ml of washing buffer. and centrifuged at 1200 MPR for 5 minutes, after which each cell sample was washed in 1300 µ to 1500 µ of washing buffer. The donor suspension was ionized and analyzed by flow cytometry.

Results: According to the mentioned cases, it can be said that mesenchymal stem cells pulp in adult cells. Teeth exist because after a dental injury, the dental pulp is used to repair the damaged area by building and depositing The dentin matrix initiates restorative dentinogenesis. This restorative process takes the entire life of the individual to do so. This indicates the presence of mesenchymal cells in the pulp of molar teeth and the ability to make odontoblasts is affected. The recommendations are appropriate. But in general, the potential of adult stem cells is not as high as embryonic and childhood stem cells, for this reason, for regeneration It is better to restore teeth by extracting embryonic tooth root mesenchymal cells (from the gums, especially the posterior gums). or the use of mesenchymal stem cells from milk teeth, these cells, as it was said, are not suitable for any category and The age group is not limited and even the ability to donate these cells from

one person to another is possible and the condition of donating teeth The complete health of the person and the donor's teeth, which can be done even in adults, which most people They have lost their milk teeth (except for latent temporary teeth) from the gene of mesenchymal stem cells of children or fetuses. Use to repair and restore teeth In the laboratory method of mesenchymal stem cells in adults, although they have the possibility of repair or regeneration, but after When they are separated from the patient, they must first go to the laboratory environment and after strengthening and differentiating them to another person as a recipient. Alograp or Xenograp is injected, but due to the many problems that occur during strengthening, injection, it takes a long time The lower potential and compatibility of these cells may cause problems such as early tooth decay, tooth loss, and system attack. Immunity to these cells can be created through immune response and... In this regard, it can be said to use a secondary method (Experiment: Laboratory cultivation of mesenchymal cells of milk teeth) More performance and benefit in this field of work. have And due to the problematic factors that exist in adult mesenchymal cells, this ideal protocol for humans is relatively far away.Recently, in new methods, with the discovery of a gene called DIK1, how the bone marrow cells are activated and tissue regeneration in healing. The teeth can be informed and undergo a shorter treatment period in the restoration of teeth using stem cells. (Because in two The above-mentioned test of restoration and reconstruction of teeth has gone through a relatively long period) With the activation of the stem cells, these cells can send messages to the main cells that lead to the activation of regenerative cells and Amplification helps a lot (this work is also possible by using low power lasers) as a result of these cells in the form Removing dentin (hard tooth tissue) helps a lot.

Conclusion: So it can be said that tooth regrowth is a reality, not an ideal, considering that teeth are made of two types of tissues It is formed differently, logically, making a tooth requires communication and cooperation with epithelial cells and odontogenic mesenchyme. Is Recombination of epithelial tissue and dental mesenchyme leads to tooth formation both in vitro and in vivo. Combined cells are able to organize and form individual layers and are also able to differentiate into odontoblasts and They also have amyloblasts. In order to make a complete tooth that has enamel and dentin, epithelial and mesenchymal cells respectively in collagen gel solution It is inserted and then implanted inside the oral cavity and with this technique the presence of all dental structures such as odontoblasts, Amyloblast, pulp, blood vessels, crown, root, periodontal ligament and alveolar bone are observed, so the implantation of this mass Dental (mesenchyme + epithelial cells) leads to the development of maturity and regrowth of teeth. Stem cells are vital for the physiology of dental pulps and for the response of these tissues to the

incident. Recent findings show have given that dental pulp stem cells can be used as possible therapeutic targets in cases of reversible pulpitis act Most importantly, these cells may be the main solution for the regeneration of necrotic immature permanent teeth become Such findings have the potential to fundamentally change the paradigms of conservative living pulp treatments and therapies create roots, and maybe allow in the future to treat problems that arise during the processes that occur in engineering Medicine has been passed, they will be curable. Therefore, endodontists should be aware of the potentials of this branch of endodontic reconstruction It is emerging as well as the possibility of collecting stem cells during traditional dental treatments that can be used for In the future, the treatments originating from the patient's own body should be known. Also, regarding the storage of dental stem cells, it can be said that the process of storing stem cells is taken temporary teeth and diseased wisdom teeth may be one of the strategies to understand the possibility of cell-based regeneration treatment. be the fundamental teeth. Recently, dental tissue cell storage has been planned and planned in several branches of dentistry It has been implemented in several countries. Today, we can use baby teeth to store dental stem cells Let's collect the house, which, of course, is accompanied by the following instructions: There should be blood flow when the tooth comes out - that is, some bleeding when the tooth comes out The tooth must be stored using cultured cell services so that laboratory tests can be performed on it To confirm the presence of stem cells before freezing. So it can be said that using engineering and modern methods, it is possible to use mesenchymal stem cells extracted from the pulp. Teeth and temporary teeth are used to repair tooth tissues under tissues that have mesenchyme and connective tissue and with this Humans at any age are able to regrow their teeth using the gene of mesenchymal stem cells And the point in It is worth noting that the use of mesenchyme gene is not restricted from one person to another (no age limit of people). It is that the use of this method if the mesenchyme gene used is healthy, unlike the implant, there are no restrictions And it is not harmful and replacing this method instead of today's methods, dentists can use it more economically and optimally have more.

Keywords: Mesenchymal stem cells - dental pulp - dental follicle

Substitutes of plant extracts for chemical treatments in breast cancer during pregnancy (Review)

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Introduction: Considering the prevalence of breast cancer in most countries of the world, one of the most widely used methods that help to treat cancer is CAR T cell therapy. This method can cure the disease, but it causes severe side effects and sometimes causes death. Also, we cannot use this method in the treatment of solid tumors. New synthetic molecules that provide new features to T cells are chimeric antigen receptors. Breast cancer surgery is possible in all trimesters and radiotherapy is not an obstacle after the first period of pregnancy. Chemotherapy is started from the twelfth week of pregnancy, but the targeted treatment of endocrine glands and HER2 is prohibited throughout pregnancy. Plants that contain polyphenols, brassinosteroids, and taxols have anti-cancer properties and are used in the treatment of most diseases. Polyphenols induce carcinogenesis through direct binding polyphenol-regulated acetylation, methylation, or phosphorylation. Curcumin, which is extracted from the rhizome of Curcuma longa L., is a type of polyphenol. Curcumin suppresses the expression of tumor necrosis factor (TNF) in the treatment of cancer cells in different cell groups through interaction with different stimuli. It is hoped that herbal extracts can be a substitute for chemical drugs and their harm.

Methods: The data contained in this article are taken from several articles published in full forms (original, review, and case reports/series studies) from Google Scholar from 2019 to 2023 And the subjects that changed the main axis were removed.

Results: By evaluating the information obtained from the physical examination of the breast in connection with pregnancy or breastfeeding, the diagnosis of breast cancer can be made easier, because the hormones of pregnancy lead to an increase in the size of the breast, an increase in the density and firmness of the breasts. Treatment through CAR T cells is a complex process that deals with several steps such as manufacturing CAR T cells, lymphatic chemotherapy, injection of therapeutic cells, and management of short-term or long-term toxicities. Creating the potential of life-threatening

toxicities, production of specific pathogenic products, high cost, and incomplete response to the disease are other disadvantages of this method. Through the binding property of nanobodies, we can design chimeric receptors so that engineered T cells with receptors have high detection power in identifying breast cancer cells. This method cannot be used in solid tumors in blood malignancies, the cellular level of the c-Met molecule was expressed in 50% of breast tumors. During pregnancy, curcumin protects trophoblast cells, reduces oxidative stress, and improves pregnancy. Also, curcumin is used as an alternative treatment for GDM. Curcumin can prevent FGR-induced inflammation and insulin resistance by regulating insulin signaling pathways. PGMD nanoparticles trap curcumin and increase its bioavailability to breast cancer cell lines. Nanoparticles with a size of less than 200 nm can last longer in blood circulation and accumulate in tumor areas. These particles facilitate absorption by cancer cells.

Conclusion: The drugs used during hormone therapy are harmful to the developing fetus. Treatment of breast cancer in women causes a severe decrease in fertility and increasing age increases its probability. Curcumin is used in the treatment of various cancers, including breast cancer in pregnant women, to overcome the chemical disadvantages of other methods such as car T-cell therapy.

Keywords: Breast cancer, Fertility, Car T cells, Curcumin

Sugar-Rich Foods Carry Osmotolerant Yeasts with Intracellular Helicobacter Pylori and Staphylococcus spp (Research Paper)

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1.

Introduction: The gastrointestinal tract is the main portal of entry into the human body for food- and water-borne microorganisms. Helicobacter pylori (H. pylori) is a bacterium involved in peptic diseases with unknown environmental sources and route of transmission.1 On the one hand, close contact is believed to be the main route of transmission of H. pylori, which occurs from mother to child and among siblings.2 On the other hand, H. pylori is considered as a gastric colonizer whose entry into the human stomach may occur along with the inges tion of food and water.3 However, there is no convincing evidence to indicate the survival of H. pylori in food 4 and water.5 It has been suggested that food processing steps exert physical and chemical stresses on H. pylori, and thus different foods cannot be considered as vehicles for carrying H. pylori to the human gastrointestinal tract.6 Furthermore, several reports demonstrated that H. pylori inside foodborne yeast could be protected from stressful conditions present in different food materials.7 On the other hand, Staphylococcus spp. are typically found in both fermented and non-fermented animal and plant foods.8 The coexistence of Staphylococcus and yeast has been frequently reported, for example, in food and microbial biofilms.9 A clinically significant yet not fully elucidated fungal-bacterial interaction is the one occurring between Candida albicans and Staphylococcus spp.10 Yeasts are ubiquitous unicellular fungi that live as saprophytes on plant or animal materials, preferential ly using sugars as carbon and energy sources.11 Yeasts are equipped with different hydrolytic enzymes, such as glycosidases, cellulases, proteinases, and lipases,11-13 which enable them to use different kinds of substrates and thus thrive in a wide range of environmental niches. Reports indicate that compared with bacteria, yeasts are more tolerant of stressful conditions such as acidic pH and are also able to grow in a wider range of water activity.14 Sugar-rich foods with low water activity are considered to be stressful materials that are hostile to microbial life, causing bacterial death due to osmotic shock.15 However, osmotolerant yeasts not only tolerate the osmotic shock but are capable of growing under such conditions. It has been demonstrated that osmotolerant yeasts accumulate glycerol or other polyols in response to low water activ ity, maintaining or restoring an inside-directed driving force for water across their cell membrane.11 Moreover, these polyols, with their hydroxyl groups, retain intracel lular polymers in hydrated form, thus

preserving enzyme activity.16-18 Yeasts that tolerate environments with high sugar and low-water contents are osmotolerant yeasts encompassing most of the ascomycetes.19 Fresh fruits with high levels of sugars and other nutrients and intermediate (15-50%) water content provide favorable conditions for microbial growth.20 However, bacteria cannot tolerate the acidic pH of these fruits and are thus eliminated, allowing osmotolerant yeasts to multiply and become established as the normal microflora in the sweet niche of fruits.21 Dried fruits, preserved fruits, and fruit syrups are also sugar-rich foods with low water activity that carry osmotolerant yeasts as their normal microflora.14 Different kinds of sugars that are used as additives in sweet foods might also carry osmotolerant yeasts. These yeasts are common contaminants of sugar factories and those that process concentrated solutions of sugars.22 Sugars are produced from molasses of sugar beet or sugar cane that have high microbial contents, mainly consisting of bacterial spores, yeasts, and molds. Yeasts and molds do not usually survive the main steps of sugar manufacturing operations, which involve high temperatures and reduced water activity. However, airborne yeasts or those that occur on the surface of refinery equipment can recontaminate the raw sugar in the final steps, multiply, and increase their population to 104-106 per gram of sugar.23 Accordingly, most of the yeast populations in sugar products are postproduction contaminants.24 In this study, yeast isolates from sugar-rich foods, fresh fruits, dried fruits, commercial unprocessed and processed sweet foods, and miscellaneous foods were examined for the occurrence of intracellular H. pylori and Staphylococcus spp. by molecular and microscopic methods. Specific primers were used for the detection of H. pylori and Staphylococcal 16S rDNA in the total DNA of yeasts. Light and fluorescence microscopes were used for observing the live and moving bacteria inside the yeasts. Moreover, FITC (Fluorescein isothiocyanate) conjugated antibodies were used for immunodetection of H. pylori and Staphylococcus spp. inside the vacuole of yeast cells. The rationale of the study was to demonstrate that yeasts in popular sugar-rich foods may serve as reservoirs of H. pylori and Staphylococcus, facilitating their spread within human populations

Methods: Collection and culture of samples Sixty samples were collected from high-sugar foods and classified into four groups: fresh fruits (×15): blackberry, apple, grape, persimmon, peach, fig, banana, white dragon, red dragon, Saturn peach, strawberry, carrot, plum, and cantaloupe; dried fruits (×15): whole date, heart of palm, date cube, raisin, and dried apricot; processed and un processed commercial foods (×22): brown sugar, icing sugar, quince jam, date syrup, sugarcane syrup, sugarcane foam, cooked beets, kombucha tea, white sugar, sugar cube, cinnamon-flavored sugar cube, low-calorie sweetener, Gaz (traditional Persian sweet), rock candy, black grape syrup, white grape syrup, plain biscuit, and Iranian delight;

miscellaneous foods (×8): pistachio, almond, cashew nut, walnut, old pickled garlic, and old pickled garlic syrup. One gram of each food material was inoculated into 3 mL of brain heart infusion (BHI) broth (Merck, Germany) and incubated at 30ºC for 7-10 days. A 50- µL volume of each BHI broth was surface inoculated on YGC (0.5% yeast extract, 2% glucose, 0.01% chloram phenicol, and 1.5% agar) and observed for the growth of yeast after 24-48 hours of incubation at 30ºC. Isolation of yeasts A single colony was selected from each of the 32 yeast-positive cultures and sub-cultured more than 10 times on YGC agar to ensure the absence of bacterial contamination. Fresh cultures of yeasts were used for gram staining and observation of the typical morphology of yeasts by light microscopy. PCR-restriction fragment length polymorphism (RFLP) of the internal transcribed spacer (ITS) region in 5.8S rDNA Fresh cultures of yeasts were used for the extraction of DNA.25 The primer pair used to amplify the ITS region was ITS-1 (5'-TCCGTAGGTGAACCTGCGG-3') and ITS-4 (5'-TCCTCCGCTTATTGATATGC-3').26 Amplification was performed with yeast DNA as a template and initial denaturation at 94ºC for 5 min, followed by 35 cycles of denaturation at 94ºC for 1 min, annealing at 55ºC for 1 min, and extension at 72ºC for 2 min, and a final extension at 72ºC for 10 min. PCR products were electrophoresed using 1% agarose gel in Tris-borate EDTA (TBE) buffer (0.5x) and digested without fur ther purification, using restriction endonucleases HhaI (Promega, USA), HaeIII and HinfI (Bioron, Germany). Restriction fragments were electrophoresed using 2% agarose, and the size of fragments was determined according to a 50-1500 bp molecular ladder. Yeasts were classified into 13 groups according to their RFLP pattern.26 Amplification and sequencing of 26S rDNA Amplification of the D1/D2 region of 26S rDNA of the 32 yeasts was carried out using primers NL1 (5'-GCATATCAATAAGCGGAGGAAAAG-3') and NL4 (5'-GGTCCGTGTTTCAAGACGG-3').27 PCR was performed with initial denaturation at 94º C for 1 min followed by 35 cycles of denaturation at 94ºC for 1 min, annealing at 50ºC for 1 min, and extension at 72ºC for 2 min with final extension at 72ºC for 5 min. After electrophoresis, PCR products of representatives of the 13 RFLP groups with a size of 600 bp were purified, sequenced, and matched with published sequences in GenBank by using the BLAST program (https://blast. ncbi.nlm.nih.gov). Light and fluorescence microscopy for observation of intracellular bacteria Wet mounts were prepared from fresh cultures of the 32 yeasts on YGC agar and examined by light microscopy to observe the moving bacteria inside the vacuoles of yeasts. Furthermore, to find out whether bacteria were alive, a fresh culture of a yeast isolate was used for staining with the LIVE/DEAD BacLight Bacterial Viability Kit (L-7012; Molecular Probes, USA) according to the manufacturer's instructions. A wet mount was examined by a fluorescence microscope (Olympus, Tokyo, Japan), and photographs were taken at different time

intervals. Detection of H. pylori-specific 16S rDNA in yeasts Total DNA from 32 yeast isolates was examined for the presence of H. pylori-specific 16S rDNA. PCR was carried out using primers HP1: 5'-GCAATCAGCGT CAGTAATGTTC-3' and HP2: 5'-GCTAAGAGAT CAGCCTATGTCC-3'.28 A clinical isolate of H. pylori that was previously identified by amplification and sequencing of H. pylori-specific 16S rDNA was used as a positive control. PCR reaction mixture without template was used as a negative control. PCR was started with 94°C for 3 min and 33 cycles of 94°C for 45 s, 57°C for 184 Osmotolerant Yeasts Carry Intracellular Bacteria Middle East J Dig Dis/ Vol.12/ No.3/ July 2020 1 min and 72°C for 1 min, followed by 72°C for 5 min. PCR products were electrophoresed using 1% agarose gel, and their size was determined using a 50-1500 bp DNA ladder. Detection of Staphylococcus-specific 16S rDNA in yeasts Amplification of Staphylococcus-specific 16S rDNA was performed using the primers 16S-F 5-AACTCTGTTATTAGGGAAGAACA-3,29 and 16S-R 5'-CCACCTTCCTCCGGTTTGTCACC-3.30 The PCR program consisted of an initial denaturation step at 94°C for 10 min, followed by 35 cycles of denaturation at 94°C for 45s, annealing at 54°C for 45s and extension at 72°C for 75s, and a final extension step for 10 min at 72°C. A clinical isolate of Staphylococcus aureus, which was previously identified by amplification and sequencing of Staphylococcus-specific 16S rDNA, was used as a posi tive control. PCR reaction mixture without template was used as a negative control. The size of PCR product was de termined as above. The PCR product amplified from the Candida parapsilosis isolate was purified, sequenced, and matched with published sequences of Staphylococcus spp. in GenBank. Results of sequence analysis showed 99% similarity to Staphylococcus succinus. Localization of H. pylori and Staphylococcus spp. inside the yeast vacuole using direct immunofluorescence assay Localization of H. pylori and Staphylococcus spp. inside the vacuole of C. parapsilosis was performed by direct immunofluorescence (IF) assay. FITC-conjugated IgY-HP prepared against H. pylori in hen,31 and FITC conjugated IgG-ST prepared against Staphylococcus spp. in rabbit,32 were used for detection of H. pylori and Staphylococcus spp. inside the yeast's vacuole. IF assay was performed according to Hašek.33 A fresh culture of yeast in YG (0.5% yeast extract and 2% glucose) broth, was fixed with 7.4% paraformaldehyde for 120 min while shaking. After washing with 0.1 M potassium phosphate citrate buffer (KCP), fixed cells were permeabilized using lyticase (L4025; Sigma) and Triton X-100. Cells were washed and resuspended in 0.4 M PIPES buffer containing FITC-labeled antibodies and 0.01% evans blue solution (for color contrast) and incubated at room temperature for 60 min. After washing three times with PIPES, a 10-µL volume of yeast suspension was smeared onto a glass slide, air-dried, covered with mounting oil (Invit rogen, USA) and examined by fluorescence microscopy. Fresh cultures of H. pylori and Staphylococcus

aureus were used as positive controls. A negative control yeast (a yeast with no amplification of H. pylori and Staphylo coccus 16S rDNA) was used to demonstrate the lack of non-specific interaction of antibodies.

Results: Isolation of yeasts Microscopic examination of gram-stained smears of yeast colonies on YGC agar showed typical yeast morphology. Of 60 samples, 32 (53.3%) were positive for yeast growth. Yeast-positive samples included 10 of 15 (66.6%) fresh fruits, 8 of 15 (53.3%) dried fruits, 11 of 22 (50%) commercial foods, and 3 out of 8 (37.5%) miscellaneous foods. Molecular identification of yeasts Amplification of the ITS region of 5.8S rDNA from the 32 yeasts revealed bands with a size of 370 to 880 bp, which were digested with restriction endonucleases. Yeasts were classified into 13 groups according to their PCR-RFLP pattern. RFLP group 12 with five isolates of C. albicans, group 8 with four isolates of Meyerozyma guilliermondii, group 5 with four isolates of Candida diversa, and group 1 with four isolates of Pichia kudriavzevii contained the highest number of yeast isolates. In the fresh fruits group, isolated yeasts included Zygosaccharomyces bailii (×2), P. kudriavzevii (×2), Pichia pastoris (×1), Zygosaccharomyces mellis (×1), Metschnikowia pulcherrima (×1), C. diversa (×1), and Candida catenulata (×2) (table 1). In the dried fruits group, isolated yeasts included P. kudriavzevii (×1), Meyerozyma guilliermondii (×3), Sac charomyces cerevisiae (×1), C. parapsilosis (×2), and Wickerhamomyces anomalus (×1) (table 2). In the com mercial foods group, isolated yeasts included C. al bicans (×3), Meyerozyma guilliermondii (×1), P. kudria vzevii (×1), Saccharomyces cerevisiae (×2), C. diversa (×2), C. parapsilosis (×1), and Yarrowia lipolytica (×1) (table 3). In the miscellaneous foods, isolated yeasts included C. albicans (×2) and C. diversa (×1) (table 4). Siavoshi et al. 185 Middle East J Dig Dis/ Vol.12/ No.3/ July 2020 186 Osmotolerant Yeasts Carry Intracellular Bacteria Table 1: Frequency of Helicobacter pylori 16s rDNA and Staphylococcus 16s rDNA in 10 yeast isolates from fresh fruits Samples RFLP group Sequencing result (26S rDNA) H. pylori 16S rDNA Staphylococci 16S rDNA Blackberry 2 1 P. kudriavzevii - - Strawberry 2 Z. bailii + - Grape 3 Z. mellis - - Persimmon 4 M. pulcherima - - Peach 2 Z. bailii + - Fig 5 C. diversa + - Banana 6 P. pastoris + - White dragon 7 C. catenulata + - Red dragon 7 C. catenulata + - Carrot 1 P. kudriavzevii + - Table 2: Frequency of Helicobacter pylori 16s rDNA and Staphylococcus 16s rDNA in eight yeast isolates from dried fruits Samples RFLP group Sequencing result (26S rDNA) H. pylori 16S rDNA Staphylococci 16S rDNA Date 2 1 P. kudriavzevii - - Date 3 8 M. guilliermondii - - Date 4 9 S. cerevisiae + + Date 5 8 M. guilliermondii + + Date 6 10 W. anomalus + + Date 7 11 C. parapsilosis + + Date 8 11 C. parapsilosis + + Heart of palm 8 M. guilliermondii + - Table 3: Frequency of Helicobacter pylori 16s rDNA and Staphylococcus 16s rDNA in 11 yeast isolates from processed and unprocessed commercial foods Samples RFLP

group Sequencing result (26S rDNA) H. pylori 16S rDNA Staphylococci 16S rDNA Brown sugar 1 12 C. albicans + - Brown sugar 2 12 C. albicans + - Icing sugar 8 M. guilliermondii - + Quince jam 1 P. kudriavzevii + - Date syrup 13 Y. lipolytica + - Sugarcane syrup 12 C. albicans + - Sugarcane foam 9 S. cerevisiae + - Cooked beet 1 5 C. diversa - + Cooked beet 2 11 C. parapsilosis + - Cooked beet 3 5 C. diversa + - Kombucha tea 9 S. cerevisiae + + Table 4: Frequency of Helicobacter pylori 16s rDNA and Staphylococcus 16s rDNA in three yeast isolates from miscellaneous samples Samples RFLP group Sequencing result (26S rDNA) H. pylori 16S rDNA Staphylococci 16S rDNA Pistachio 5 C. diversa + - Old pickled garlic 12 C. albicans - - Old pickled garlic syrup 12 C. albicans - - Middle East J Dig Dis/ Vol.12/ No.3/ July 2020 Light and fluorescence microscopy of yeast Light microscopic examination of wet mounts pre pared from cultures of the 32 isolated yeasts showed the occurrence of bacteria inside the vacuole of all the yeast cells (Fig.1 A). Live/Dead staining of yeast cells con firmed the viability of intracellular bacteria (Fig.1 B). Photographs taken from a stained wet mount of yeast, at three-time intervals, showed live and moving bacteria inside the yeast cell vacuole (Fig.1 C1-C3). Detection of H. pylori- and Staphylococcus-specific 16S rDNA in yeasts The amplified product of H. pylori-specific 16S rDNA with a size of 521 bp was detected in 23 of 32 (71.8%) yeast isolates. The frequency of H. pylori-positive yeasts in different groups of samples was determined to be 70% (7out of 10) in the fresh fruits group: Z. bailii (×2), C. diversa (×1), P. pastoris (×1), C. catenulate (×2), and P. kudriavzevii (×1) (table 1); 75% (6 out of 8) in the dried fruits group: Meyerozyma guilliermondii (×2), C. parapsilosis (×2), W. anomalus (×1) and Saccharomy ces cerevisiae (×1) (table 2); 81.8% (9 out of 11) in the commercial foods group: C. albicans (×3), P. kudriavzevii (×1), Y. lipolytica (×1), Saccharomyces cerevisiae (×2), C. diversa (×1), and C. parapsilosis (×1) (table 3); and 33.3% (1 out of 3) in miscellaneous foods: C. diversa (×1) (table 4). Staphylococcus-specific 16S rDNA with a size of 750 bp was detected in 22.2% (8 out of 36) of yeast isolates. The frequency of Staphylococcus spp.- positive yeasts was determined to be 62.5% (5 out of 8) in the dried fruits group (Saccharomyces cerevisiae, Meyerozyma guilliermondii, W. anomalus, and 2× C. parapsilosis) and 27% (3 out of 11) in the commercial foods group (Saccharomyces cerevisiae, Meyerozyma guilliermondii and C. diversa) (tables 2 and 3). Yeast iso lates from fresh fruits, and miscellaneous foods did not carry Staphylococcus-specific 16S rDNA (tables 1 and 4). The frequency of yeasts containing both H. pylori and Siavoshi et al. 187 Fig.1: Light and fluorescence microscopy of yeast. A) Light microscopy of yeast cells shows intracellular bacteria (IB) inside yeast's vacuole (V). B) Live intracellular bacteria (IB) appeared as green spots in the vacuole (V) of stained yeast cells. C1-C3) Photographs taken at three-time intervals (0, 5, and 10 seconds) show the moving bacteria. Original magnification x 1000. Middle East J Dig Dis/ Vol.12/

No.3/ July 2020 Staphylococcus spp. was 62.5% in dried fruits and 9% in commercial foods. Altogether, among the 32 isolated yeasts, 17 (53%) were H. pylori-positive only, two (6%) were Staphylococcus spp.-positive only, six (18.7%) were positive for both H. pylori and Staphylococcus spp., and seven (21.8%) were negative for both. Localization of H. pylori and Staphylococcus spp. inside the yeast vacuole using direct immunofluorescence assay Specific interaction of FITC-IgY-HP (Fig.2, B and C) or FITC-IgG-ST (Fig.2, F and G) with intracellular bacteria confirmed the identity of bacteria as H. pylori or Staphylococcus spp. and their localization inside yeast's vacuole. Dark vacuole of negative control yeast without fluorescent spots indicated the lack of non-specific interaction of antibodies (Fig.2, D and H)

Conclusion: Carbohydrates are the most popular foods consumed by humans worldwide. In addition to be a major carbon source for building living cells, their sweet taste, and energy sion afford these compounds a very special place in the human diet. Sweet foods are recognized as comfort foods because their consumption leads to elevation of serotonin, the known anti-depressant neurotransmitter that reduces pain and regulates sleep and the biological clock.34 Sugars are also used to improve the quality of foods due to their functional properties.35 Furthermore, sugar and salt are the oldest preservatives that, when added to food materials, protect them against microbial spoilage by producing high osmotic pressure. Accordingly, sugars are frequently added to a variety of foods and beverages. Bacteria cannot withstand the osmotic stress of sugar-rich environments and die, while osmotolerant yeasts survive and even multiply.36 Fresh and dried fruits, fruit juice, and refined sugar products are sugar-rich environments of plant origin that cause stress to microbial cells by reducing water activity, changing cell turgor pressure, and destabilizing macro molecules.15 This might indicate that floral nectar and fruits have evolved to accumulate high concentrations of sugar to protect the fertile parts of plants from microbial attack.37,38 However, osmotolerant yeasts that show maximum fitness in high concentrations of sugars,39 increase their population and become established as the normal microflora of such sugar-rich plant environments, including floral nectar and fruits.40 These symbiotic yeasts, while feeding on plants, stimulate plant metabolism, and inhibit phytopathogens.41,42 Insects, which play an important role in pollination and reproduction of plants, feed on yeasts and carry them from the soil to plants and disperse them within plants during pollination.43 It appears that symbiosis of yeasts with insects and plants is an important and inevitable evolutionary event.44 Accordingly, yeasts as permanent associates of plants, enter the human digestive system through the consumption of sugar-rich and plant derived food products. Yeasts with high potential for genotypic 45,46 and phenotypic 47 plasticity are permanent symbiotic inhabit ants of plants,41,42 insects,48 animals,49 and humans 50

in a wide range of environments.37,51 Accordingly, it is not surprising that fungi with these sophisticated properties have evolved to serve as a unique niche for sheltering the endosymbiotic bacteria.52 In our previous studies, H. pylori-specific genes were detected in oral,53 gas tric,54 vaginal,55 and foodborne 7 yeasts. Furthermore, H. pylori-specific proteins were detected in the protein pool of gastric yeasts by western blot technique,56 and intra cellular H. pylori was localized in the vacuole of Can dida yeast by FITC-IgY-HP.31 Results of similar studies performed in our lab showed the detection of Staphylococ cus- specific genes 57 and proteins 32 in gastric yeasts as well as staphylococcal localization inside the vacuole of gastric yeast by immunodetection and FISH methods.32 It was proposed that inside the vacuole of Candida yeast, H. pylori, or Staphylococcus are protected from environ mental stresses and provided with nutrients for survival and multiplication. Accordingly, yeast was suggested as a potent reservoir of H. pylori and Staphylococcus. 7,53,54,58 Among the 32 yeasts isolated in this study, 17 (53%) were H. pylori-positive only, two (6%) were Staphy lococcus spp.-positive only, six (18.7%) were positive for both H. pylori and Staphylococcus spp., and seven (21.8%) were negative for both bacteria. Among the sugar rich foods studied, dates showed the greatest potential for supporting intracellular H. pylori (75%) and Staphylo coccus spp. (62.5%), or both (62.5%) in yeasts. The frequency of H. pylori-positive yeasts in fresh fruits, dried fruits, and commercial foods was 70–81.8%. Fresh fruits contain high levels of sugars, other nutrients, and intermediate water activity that favor microbial growth. However, acidic pH eliminates bacteria and provides appropriate conditions for fungal growth. The natural microbiota of fruits is commonly composed of yeasts such as Candida, Pichia, Saccharomyces, Hanseniaspora, and Zygosaccharomyces.21 Dried fruits such as date fruits, in addition to sugar, contain salts and minerals, fatty acids, amino acids, proteins, and vitamins, including B1, B2, and B3. Furthermore, dates are rich in different kinds of sterols 59,60 that are precursors of ergosterol involved in the synthesis of yeast membranes.61 It is notewor thy that sterols also serve as precursors of cholesterol, an important constituent of H. pylori cell membrane.62 Commercial foods such as sugar cubes, granulated white and brown sugars, and other related high-sugar products are frequently used as sweet additives to tea, coffee, and sherbets or to formulated foods such as desserts and pastries. These compounds with high sugar content could carry yeasts either of plant origin or introduced as post-operation contaminants.63 Among the miscellaneous foods investigated, the two C. albicans isolates from old pickled garlic, and old pickled garlic syrup did not contain H. pylori or Staphylococcus spp. However, the three C. albicans isolates from com mercial foods, and eight out of nine Candida spp. from other foods carried H. pylori. This might indicate that long storage of pickled garlic in vinegar, although favoring the survival of C. albicans yeasts, could exert a

negative effect on the survival of intracellular bacteria, leading to a reduction in bacterial copy number such that bacterial DNA was not detectable by PCR. Negative PCR results have been suggested to result from failure in the detection of bacterial genes due to low bacterial copy number, inadequate amount of extracted DNA,64 or lack of primer recognition sites in bacterial DNA due to variation in the target sequence.65 Results of this study showed that sugar-rich foods, whether naturally sweet or containing added sugar, are carriers of osmotolerant yeasts that could contain H. pylori Siavoshi et al. 189 Middle East J Dig Dis/ Vol.12/ No.3/ July 2020 and/or Staphylococcus spp. Detection of H. pylori- and/ or Staphylococcus-specific genes shows the probable occurrence of multiple endosymbiotic bacteria in the vacuoles of yeasts with different frequencies. Microscopic observations of bacteria in new generations of yeasts along with amplification of H. pylori- and Staphylococcus specific genes from consecutive generations indicate that new yeast cells can inherit the intracellular bacteria as part of their vacuolar content. Extensive studies on the intracellular existence of non-culturable bacteria inside arbuscular mycorrhizal fungi indicated that the fungal vacuole provided a nourishing and protective niche for the endosymbiotic bacterium 'Candidatus Glomeribacter gigasporarum' (CaGg), facilitating its replication and transmission to the next generation.52 Moreover, the occurrence of two types of endosymbiotic bacteria has been reported in arbuscular mycorrhizal fungi: the gram negative beta proteobacterium CaGg, and a gram-positive molicutes-related endobacterium. 66 It is noteworthy that microscopic observation of bacterial structures inside the vacuoles of yeast isolates with negative results for amplification of H. pylori or Staphylococcus genes suggests the likelihood of the occurrence of other intracellular bacteria yet to be identified. Yeasts enter the food cycle of animals, including humans, through the consumption of sugar-rich and plant-derived foods. Yeasts are able to survive in the human gastro intestinal tract due to their high potential to adapt to different stressful conditions and return to natural soils when excreted. It can be concluded that different yeasts that occur in the soil are more or less representatives of the yeast populations of plant and animal life above the soil surface. In this fashion, yeasts establish more or less similar populations in soils, plants, and animals, including humans. In all the steps of the food cycle, yeast may carry its intracellular bacteria and spread it to different hosts such as insects, plants, and animals. Accordingly, the intracellular occurrence of H. pylori, Staphylococcus spp. and probably other bacteria inside the yeast could be regarded as a sophisticated survival strategy of bacteria that evolved along the evolutionary path. Overall, yeasts may be regarded as permanent reservoirs of bacteria, and thus bacteria will exist as long as yeasts persist

Keywords: Osmotolerant Yeasts Carry Intracellular Bacteria

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Surface modification of PES fibers for biocompatibility (Review)

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Introduction: Polyethersulphone (PES) is one of the most important polymers with many desirable properties like exceptional mechanical properties, chemical stability, and so on. For these reasons, it is used as a biomaterial in medicine. One of the clinical applications of PES is in haemodialysis membranes. PES has also been used as scaffolding in some projects. On the other hand, PES is very hydrophilic and therefore has some problems. When it comes into contact with blood, some proteins attach to its surface and the biocompatibility and haemocompatibility properties of the polymer are reduced. There are many surface modification methods to improve biocompatibility and cell properties. This study reviewed the previous studies on surface modification of PES.

Methods: Chua et al compared the expansion of human umbilical cord blood CD34+ cells on unmodified, hydroxylated, carboxylated, and aminated PES nanofibers. The results of the ten-day culture showed an increase in the growth of cells on the aminated fibers. Another research study was on the bioartificial kidney. In this study, PES fibers coated by L-3, 4-dihydroxyphenylalanine, and human collagen type IV to improve proliferation of human embryonic kidney cells-293 (HEK-293) and separation of uremic toxins. The result showed low hemolysis, prolonged blood coagulation time, and minimal platelet adhesion. These results demonstrated that these coated PES fibers can be a potential biocompatible substrate for the attachment and proliferation of HEK-293 cells and the removal of uremic toxins from the simulated blood. Modification of PES fibers with a peptide sequence based on fibronectin was performed by Lin et al. The attachment and proliferation of adipose-derived stem cells was assessed and RGD-treated surfaces resulted in a higher proliferation of ASCs after 6 and 48 h. These results indicate that PES membranes modified with the RGD peptide sequence can be utilized for enhanced cell attachment in biomedical applications. In a research that Was performed by Hashemi et al, PES fibers were modified by collagen, and mouse embryonic stem cell proliferation was tested. The results indicated the enhanced infiltration and teratoma formation of cells in modified PES. In one study, PES fibers coated with glutaraldehyde-crosslinked gelatine were produced by the dry-wet spinning method using a triple orifice spinneret. The

results of in vitro haemocompatibility tests showed better blood compatibility on modified PES. HepG2/C3A cells cultured on days 3 and 6 showed better cell attachment and proliferation. This study shows that these fibers are a suitable substrate for hepatocyte culture. Seyedjafari et al also coated PES fibers with collagen for liver tissue engineering. Human bone marrow-derived stem cells are seeded on this fiber. cell-seeded scaffolds after 7 days of culture were tested by MTT assay. The results showed normal attachment and proliferation on modified PES fibers. Polyethersulfone fibers were chemically modified by covalent coupling with lactobionic acid. The hemocompatibility test indicated the suitability of the modified membranes with human blood. Human primary mesenchymal stem cells and HepG2 cells were cultured on modified PES and the result showed suitable cell proliferation and growth. In another study, the surface of PES fibers was modified by fluorapatite nanoparticles. MTT test showed suitable proliferation, and attachment of human bone marrow mesenchymal stem cells on modified PES fibers. The result showed that these modified fibers helped with biocalcification and osteogenesis. In the research of Shabani et al, PES fibers were surface-modified by plasma treatment and collagen grafting. Stem cells were cultured on modified fibers and this test showed normal morphology of the cell.

Results: The results of previous research have shown that coating the surface of polyethersulfone fibers reduces the hydrophobicity of the surface, which increases coagulation time, reduces platelet adhesion, and improves blood compatibility. In cell culture, this also increases the biocompatibility, adhesion, and growth of cells.

Conclusion: Polyethersulfone has been used as a biomaterial because of its unique properties. It has been used as a scaffold for stem cells, liver, etc. However, the problem of hydrophobicity has limited its use. As described above, by modifying the surface, it is possible to improve the hydrophobic properties and consequently its biocompatibility. Considering that polyethersulfone is a commercial polymer, research is still ongoing, and more clinical and in vivo studies are needed to modify its surface.

Keywords: Polyethersulfone, Surface modification, Hemocompatibility, biocompatibility

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Surrogacy; Ethical and Legal Challenges (Review)

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Introduction: Based on the World Health Organization (WHO) report, approximately 17.5% of the world population experience infertility. Assisted reproductive methods include drug treatment, surgical procedures, intrauterine insemination (IUI), In Vitro Fertilization (IVF), intracytoplasmic sperm injection or microinjection (ICSI), and donation . In the donation method, various subtypes such as surrogate uterus, embryo donation, ovum donation, and sperm donation are done . Surrogacy is an assisted reproductive method, in which traditional and gestational are its subtypes. The use of surrogacy has increased until now, and among all Assisted Reproductive Technologies (ART) in the United States of America, about 1.9% of births are due to surrogacy.

Methods: To determine the scope of this review, we searched in databases such as "pubmed", "Scopus", "Web of Science" with the keywords "surrogacy", "ethic", "legal" and other related MeSH terms up to September 2023. All of results included into our study for highliting the ethical and legal challenges of surrogacy.

Results: Although surrogacy is being done widely, some ethical and legal challenges exist. In some countries such as Ukraine, Greece, and Georgia, a surrogate receives a sum from the intended parents, recognized as “commercial surrogacy”. At the same time, commercial surrogacy is illegal in other countries, such as Italy, Spain, and the United Kingdom. In some other countries like Saudi Arabia, the United Arab Emirates, France, Germany, Austria, and Japan, all types of surrogacy are illegal. Beyond the legal status of surrogacy in countries, the ethical challenges of surrogacy are essential. Risks associated with delivery and pregnancy for a surrogate, autonomy, and access to care of surrogate, psychological problems of intended parents and surrogate, congenital disabilities of the child, child rights, intra-family sex cell donation, and gender discrimination are a few numbers of existing problems

Conclusion: The mentioned problems may have worse effects on surrogacy and reduce the rate of birth from this assisted reproductive method. Thus, the necessity of international regulation for surrogacy, determining risks and problems for surrogates and parents to reduce controversies between parties.

Keywords: surrogacy, ethics, legal

Symmetry study of dermatoglyphic patterns in the first phalanx thumb of left and right hand in a population of Persian women with rheumatoid arthritis living in Razavi Khorasan province (Research Paper)

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Introduction: Symmetry has emerged as a morphological-anthropometric feature in order to establish the body's axes during the embryonic period. Dermatoglyphic is a science that deals with the correct and fundamental study of the skin lines on the palms, feet, and fingertips. Study of the asymmetry and status of dermatoglyphic patterns in the fingers can be related to the occurrence of disorders such as cancers and syndromes and chromosomal and non-chromosomal diseases. Since the relationship between the arrangements of the lines of the fingertips has been proven in some diseases such as schizophrenia, Alzheimer's, asthma, etc. Analysis of the type of skin lines is used as a research-diagnostic method in medicine for the early recognition of many diseases. Rheumatoid arthritis is an unknown chronic inflammatory injury which can involve all body joints. The early diagnosis of rheumatoid arthritis is important in the treatment of this disease.

Methods: In this paper we attempt to investigate the possibility of asymmetry existence in different skin lines of first finger hint phalange of women suffering from rheumatoid arthritis. For this purpose, the print of first phalange of the left and right hand finger hint of 37 women suffering from joint rheumatoid and 79 healthy Persian women were obtained with scanner in province of Razavi Khorasan. To evaluate symmetry in line numeration of patients finger hint, we have used dependent t-test, while in qualitative studies of fingertip patterns, we have applied X2 test.

Results: Results show that there isn't a significant correlation between fingertip patterns and hand direction. In other word, distribution of fingertip

pattern in right and left hands of patients are the same. The maximum frequency of dermatoglyphic pattern was reported in both groups Loop, Whorls and Arches, respectively. A significant difference was observed between the average line numeration in the first phalanx of the right and left thumb of patients compared to healthy people.

Conclusion: Generally, we can conclude that establishment of the present study, developing basic dermatoglyphic science, is useful in the prognosis and therapeutic programming of diseases.

Keywords: Biometry, dermatoglyphic, Symmetry Gauge, rheumatoid arthritis

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Synthesis and characterization of Nano- Composite mats containing Zein and hydroxyapatite for bone tissue engineering (Research Paper)

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Introduction: Fractures, trauma, inherited bone abnormalities, and tumor excision all lead to bone defects. Nanofibrous scaffolds are preferable tissue regeneration candidates because they mimic extracellular matrix. hydroxyapatite is a bio-ceramic that belongs to the calcium phosphate family, it makes up a significant percentage of bone. Zein is a natural, biocompatible, and biodegradable polymer that has received FDA approval. In this study, we prepared composite nanofibrous scaffolds containing Zein and hydroxyapatite and we evaluated their morphology, bioactivity, and biocompatibility.

Methods: In this study, we manufactured Zein Nanofibrous scaffolds containing 5% (w/v) HA by electrospinning method. Scaffold morphology and bioactivity were characterized by scanning electron microscope, following that scaffolds were seeded by MG-63, and incubated in a 37℃ incubator for 5 days. In the next step, Nanofibrous mats were fixed with paraformaldehyde 4% and observed with SEM.

Results: The SEM results showed that the nanofibrous morphology is smooth, cylindrical and beads bid-free in all experimental groups. The Hydroxycarbonate Apatite Crystals Accumulated on Surface Scaffolds, as shown by SEM Images of Bioactivity Assessment. Moreover, MG-63 cells adhered and proliferated on nanocomposite scaffolds.

Conclusion: based on our results, the manufactured scaffolds are biocompatible, bio-adhesive, and bioactive with porous and smooth structures appropriate for tissue engineering

Keywords: Tissue engineering, Hydroxyapatite, Zein, Nanofiber

Synthesis and preparation of biuret mPEG- PCL copolymeric nanoparticle to enhance its drug delivery and anti-convulsing effect in mice (Research Paper)

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Introduction: In recent years, biuret derivatives have been studied due to their multiple biological effects, including analgesic[1], anti-inflammatory[2], anti-cancer[3] and etc. According to recent observations, the sedative effect[4] It was studied. However, due to the fact that some of the biuret derivatives are hydrophilic, their penetration through the blood-brain barrier and the emergence of their effects have become problematic or some other derivatives that are more lipophilic, the problem of dissolving them in water caused that after subcutaneous injection, their distribution in the body of the mice faced a problem and caused a weaker and delayed effect. In this study, the synthesis of such biuret derivatives and the preparation of amphiphilic nanoparticles from it to improve its pharmacokinetics and permeability and possibly improve its anticonvulsant effect.

Methods: 2.1. Synthesis of Biuret Derivative By adding potassium cyanate (KOCN) to the hydrochloride solution made from amine ureas are made, which themselves react with phenyl chloroformate in the presence of a pyridine (pyr) catalyst, they create phenyl allophanate, which reacts with another amine under reflux conditions for one night in the presence of potassium carbonate (K2CO3) to produce the desired biuret. 2.2. Preparation of Nanoparticles from Biuret Binary copolymer mPEG-PCL will be synthesized by ring-opening polymerization of caprolactone in the presence of polyethylene glycol as initiator molecule and tin octanate catalyst. Polymer nanoparticle will be prepared using nanoprecipitation method 2.3. In vivo Study of Anticonvulsant Effect In this study, four groups of NMRI adult male mice weighing 25-30 grams were used. There are 10 mice in each group. Group I-control PTZ (35mg/kg) to cause chronic seizures, group II- positive control PTZ (35 mg/kg) + phenobarbital (20 mg/kg), group III- treatment group nano biuret derivative + PTZ (35 mg/kg), and group IV- control group biuret derivative (35 mg/kg) + PTZ (35 mg/kg). In all groups, the injection was done intraperitoneally, and PTZ was injected 30 minutes after phenobarbital and biuret. In all groups, convulsive attacks are recorded 30 minutes after injection, and all abnormal animal behaviors are subclassified and scored, and finally, in order to check kindling, 10 days after the last injection, PTZ was re-injected at a dose of 75 mg/kg. and their behavior is checked for 30

minutes[5, 6]. 2.4. Analysis of Nanoparticles HNMR spectroscopy and FT-IR spectroscopy will be used to confirm and determine the structure of mPEG-PCL binary copolymer. Also, HNMR will be used to determine the average molecular mass and molecular mass distribution of mPEG-PCL binary copolymer, and DSC analysis will be used to study the thermal behavior of mPEG-PCL binary copolymer. A spectrophotometer will be used to study the amount of drug loading and drug release.

Results: The synthesis of biuret derivative was confirmed using UV/Vis, LC-Mass, IR. Also, by using DLS, TEM, IR the synthesis of nanoparticles was confirmed. According to similar articles, it was observed that biuret derivative micelles showed a better effect compared to biuret derivative itself.

Conclusion: According to previous studies and findings, the preparation of nanoparticles with mPEG-PCL copolymer can improve the pharmacokinetic and drug delivery effect of biuret derivatives, as a result, this technique can be used to improve the possible effect of other medicinal compounds with similar problems.

Keywords: biuret, nanoparticles, mPEG-PCL, drug delivery, anticonvulsant effect

Synthesis, Antimicrobial activity and Molecular Docking study of Novel 4-anilinoquinazoline derivatives. (Research Paper)

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Introduction: Nowadays, antibacterial resistance is recognized as a significant threat to health worldwide. Therefore, the search for new antibacterial drug compounds is an attractive goal for medicinal chemists . Quinazoline heterocycles are functional bioactive scaffolds in medicinal chemistry. The simple and condensed quinazoline derivatives possess diverse pharmacological activities, including anticancer , antihistaminic , antinociceptive , antithrombotic , anticonvulsant , and anti-inflammatory . Quinazolines are well known to play a significant role as inhibitors. An example is the 4-anilinoquinazoline used as an epidermal growth factor receptor (EGFR)inhibitor. Gefitinib (ZD-1839, Iressa) and erlotinib (OSI-774, Tarceva) are used as dual EGFR- human epidermal growth factor receptor 2 (HER2) inhibitors, which are used in the clinic(scheme1) . Among various pharmacological activities, quinazoline derivatives have significant antimicrobial properties. DNA gyrase is one of the interesting targets in Escherichia coli that catalyze changes in the topology of DNA and induces the formation of negative supercoils . Due to its vital role in the survival of bacterial cells and the lack of its existence in higher eukaryotes, bacterial DNA gyrase has been used as an antibacterial target. Molecular docking is used to predict the interactions between a ligand and a receptor molecule to predict ligand conformation and orientation within a targeted binding site . In the present work, we have synthesized some new derivatives of N,2-diphenylquinazolin-4-amine containing phenyl group at position 2, and various aniline derivatives at the 4th position of the quinazoline ring (Scheme 2). In addition, the antimicrobial activities of all synthesized N,2-diphenylquinazolin-4-amine derivatives were evaluated against both Gram-positive and Gram-negative bacteria as well as fungal strains. Among the compounds tested, some of N,2-diphenylquinazolin-4-amine were found to be superior in inhibiting the growth of all the bacterial and fungal strains. The synthesized derivatives were docked into the binding pocket of DNA gyrase protein, and their binding energies were calculated.

Methods: The designed compounds were prepared through the nucleophilic substitution reaction of substituted anilines with 4-chloro-2-phenylquinazoline (1) and characterized by spectroscopic methods. The antimicrobial effect of

the synthesized compounds against E. coli, P. aeruginosa, S. aureus, B. subtilis, L. rhamnosus, and C. albicans was assessed by the microdilution method. Docking experiments were performed using AutoDock 4.2. Software.

Results: The designed compounds were synthesized through the SNAr reaction of substituted anilines with 4-chloro-2-phenylquinazoline (1) as presented in Scheme 2. The reaction was done by the nucleophilic attack of NH2 to the fourth position of the quinazoline ring to displace the chlorine moiety. To explore the binding modes of the newly synthesized N,2-diphenylquinazolin-4-amine derivatives (3a-g) with the active site of E. coli DNA gyrase, a molecular docking simulation was accomplished using AutoDock 4.2. software. Firstly, chlorobiocin (the original co-crystallized ligand) was re-docked in the active site of E. coli DNA gyrase B kinase (PDB code: 1KZN) , which revealed a score energy of -6.48 kcal/mol (Table 1 and Figure 1). As shown in Fig. 1-5 and Table1, some compounds (3a, 3d, 3e, and 3f) can create a strong hydrogen bond with Asn46, Asp73, and Thr165 at a distance of 3.91 Å - 6.31 Å, which is consistent with the decomposition analysis of the electrostatic interaction. In the biological assay, the activity of the target compounds against the Gram-positive strains was more potent than their activity against the Gram-negative strains. In turn, N-(3-chlorophenyl)-2-phenylquinazolin-4-amine 3e showed potent activity against S. aureus (MIC = 0.0039 mg/mL), equal to that of the reference drug. The 1-phenyl-2-(2-phenylquinazolin-4-yl) hydrazine 3g also revealed potent activity against P. aeruginosa at 0.0625 mg/mL concentration. It seems that lipophilicity could improve the antibacterial activity of the newly synthesized N,2-diphenylquinazolin-4-amine derivatives (3a-g).

Conclusion: In this study, synthesis, molecular docking, and evaluation of the antimicrobial activity of seven novel N,2-diphenylquinazolin-4-amine derivatives were reported. All compounds showed moderate to good antibacterial activity, while remarkable antifungal activities were observed for these compounds. Computational studies were performed by automated docking of ligands to the binding sites of DNA gyrase. The results revealed that compound 3c showed minimum binding energy (-6.13 kJ/mol) and so, indicated a strong binding affinity towards DNA gyrase.

Keywords: Synthesis, quinazoline, docking, antibacterial

Targeted delivery of nucleic acids: design, preparation, impact and recent advances (Review)

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Introduction: Targeted delivery approaches for transferring therapeutic agents, especially nucleic acids, to treat certain diseases, chiefly cancers, have shown a rapid rise over the past few decades. Since the administration of nucleic acids with therapeutic potential has proved a promising approach for the treatment of several human diseases and many biological applications such as gene therapy and DNA vaccines that have already been used. Thus, on the one hand, there is a growing need for further studies on nucleic acids treatment, and on the other hand, researchers' attention is focused on the conventional methods of delivering them to the target tissue.(1-4) Considering that nucleic acids such as DNA plasmids, a variety of RNAs, oligonucleotides and synthetic nucleic acids have large dimensions and negatively charged phosphate groups within their structure and also are degradable; Therefore, their transfer to target cells requires the appropriate methods like use of viral and non-viral gene transfer systems and also physical techniques which have discussed in this article in the following. Knowing that gene therapy has the potential to replace malignant or defective genes and modify gene expression. A wide range of diseases have been studied and finally treated by gene therapy, with many cancer-related diseases, genetic disorders, neurodegenerative diseases, Alzheimer's disease and autoimmune diseases being examples of these applications. (5, 6) In the meantime, Cancer is a type of disease that is caused by numerous genetic mutations. In fact, dynamic changes in the genome and a complex network of interactions between cancer cells with different types of cells have led to cancer progression, which in turn has led to the development of tumors. It has been proven that this mechanism and process in genetic alterations that lead to a variety of diseases actually require gene therapy and sometimes it can work best to cure diseases by removing the disruption of the expression pathway of the genes involved in producing a particular protein.(7) In the last few decades,

nucleic acid delivery has shown tremendous potential for treating the aforementioned acquired and inherited diseases. In the process of gene therapy, nucleic acids, which mainly contain DNA or RNA, are transferred to the target cells for gene modification and thus to the treatment of inherited or acquired diseases. (8, 9) To understand the many uses of nucleic acids in the field of treatment, it is best to first get acquainted with the types of these macromolecules. In the beginning of this article, we have investigated the types of nucleic acids and their structure. These include oligonucleotides, aptamers, plasmid DNA (pDNA), messenger RNA(mRNA), small interfering RNA(siRNA), short hairpin RNA (shRNA) and so on. Therefore, delivery of these nucleic acids is an important strategy that represents the goal of gene therapy. Indeed, the process of delivering these nucleic acids to the target tissues and cells is that they interact with specific intermediates upon entry of the nucleic acids into the cells, which in turn leads to expression of the gene of interest or inhibition of messenger RNA (mRNA) translation in the defective gene and finally by blocking the expression of mRNA, it prevents the production of a defective protein that causes the relevant disease.(10) As a result of this movement, it provides direct treatment and intervention in the cause of the disease. (11, 12) Activity in the field of gene therapy and nucleic acid therapeutic application begun around since year 1980, but the first successful gene transfer in humans was approved by the National Health Association in year 1989 and eventually used in year 1990. (13) Since then, the number of clinical trials has gradually increased and has been globally approved. Due to the increasing successes and reports in this field, more attention has been paid by researchers to this area and trends have been steered.(14) There are several methods for nucleic acid transfer including viral and non-viral methods as well as physical methods for gene transfer. Most of the research used viral vectors as a gene delivery tool for transferring nucleic acids. The use of viral vectors has led to high levels of gene expression. Although a highly efficient and impressive method of viral transmission, due to the limitation of the potential contamination of viruses to other tissues, other methods have been included.(15) In this article we tried to address each of these methods.

Methods: With the passing of time and the advancement of science and technology in human life, consequently a change in human life style has created new relevant issues that have given new thought to the solution of these issues. One of the issues related to living in the modern world is the discussion of new diseases and related therapies. With this argument, new therapeutic approaches are needed to overcome these issues. Understanding what is happening inside the living cell and examining the chemistry of living cells is a pathway that helps researchers find the right response to the treatment of many diseases. So at first it is necessary to evaluate the

mechanisms of disease to be the well-known and proven treatment and then be sent using the right tools to the target tissue. One of the most exciting, promising, and tremendous therapeutic approaches in light of the ongoing developments is the use of nucleic acids in the treatment of new diseases in recent decades. Thus in this article at the beginning it is necessary to discuss about nucleic acid biochemical structure and different kinds of them after that investigating their therapeutic potential and finally the methods of their delivery to target tissues have been studied.

Results: With the passing of time and the advancement of science and technology in human life, consequently a change in human life style has created new relevant issues that have given new thought to the solution of these issues. One of the issues related to living in the modern world is the discussion of new diseases and related therapies. With this argument, new therapeutic approaches are needed to overcome these issues. Understanding what is happening inside the living cell and examining the chemistry of living cells is a pathway that helps researchers find the right response to the treatment of many diseases. So at first it is necessary to evaluate the mechanisms of disease to be the well-known and proven treatment and then be sent using the right tools to the target tissue. One of the most exciting, promising, and tremendous therapeutic approaches in light of the ongoing developments is the use of nucleic acids in the treatment of new diseases in recent decades. Thus in this article at the beginning it is necessary to discuss about nucleic acid biochemical structure and different kinds of them after that investigating their therapeutic potential and finally the methods of their delivery to target tissues have been studied.

Conclusion: Considering to this present article, the first step is to understand the nucleic acid structure and to identify the pharmacological effects and to select the correct vehicle for nucleic acid transfer and their effective delivery to the target tissue. The next step was to pick out the convenient and effectual method, knowing the various pathways involved in targeted delivery of nucleic acids. Nowadays the nucleic acid delivery systems are growing dramatically and are on the rise. As discussed throughout this article, it is necessary to know that all of the above mentioned methods all have both disadvantages and merits and have been used for this purpose with respect to the target cell type and nucleic acid.

Keywords: Nucleic acid delivery, Gene therapy

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Targeted delivery of SN38 to cancer cells with aptamer-functionalized exosomes (Research Paper)

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Introduction: Exosomes are classified as a type of extracellular vesicles (EV) with a size of 30-150 nm which have important role in various situations such as signaling processes, antigen presentation, immunomodulatory functions, and tumor progression. Moreover, due to some advantages over other nano-carriers such as their natural origin, higher biocompatibility and longer circulation time, exosomes have been investigated a lot in delivery of drugs and other therapeutic agents. Exosomes have been isolated from various cell sources, as well as platelets, neutrophils, macrophages, and mesenchymal stem cells (MSCs). Many studies indicated that MSCs display some prominent benefits as an exosome source, including the higher yield of exosome production, lower immunogenicity, and more stability in human plasma. Recently, using aptamers has improved functionality of exosomes in biomedical applications including targeted drug delivery. 7-ethyl-10-hydroxycamptothecin (SN38) is an anticancer member of the camptothecin family with inhibitory effect on topoisomerase 1 and it can destroy the structure and function of DNA. One of the important limitations of SN38 is its instability in a physiological pH range due to its extremely low solubility in pharmaceutical media. In this study, exosomes derived from human adipocyte mesenchymal stem cells (ADSCs) were conjugated to the MUC1 aptamer (Exo-Apt) and then loaded with SN38 using our novel combination method. So, Exo-Apt could act as a suitable carrier for efficient delivery of hydrophobic drug (SN38) to cancer cells. Afterwards, the effect of targeted and non-targeted complexes on C26 and CHO cell lines were evaluated.

Methods: First, mesenchymal stem cells were isolated from human adipocyte tissue (prepared by liposuction) and characterized. Then, the exosomes were extracted by ultracentrifugation and covalently conjugated to the amine MUC1 aptamer (Exo-Apt). Afterwards, SN38 was loaded into Exo-Apt through the novel combination method of incubation, freeze-thaw, and surfactant treatment (SN38/Exo-Apt) and its targeting potential and cytotoxic effects on cancer cells were investigated.

Results: With our novel combination method, encapsulation efficiency of SN38 into exosomes was considerably enhanced (58%). Moreover, flow cytometry results revealed the great cellular uptake of SN38/Exo-Apt in C26 cancer cells. The remarkable cytotoxicity of SN38/Exo-Apt on C26 cells was exhibited without obvious toxicity on normal CHO cells through MTT assay.

Conclusion: Our results showed that SN38 as a hydrophobic drug was loaded efficiently into the Exo-Apt using our novel approach. Conjugation of exosome with MUC1 aptamer could enhanced the cellular uptake and significantly increased the cytotoxicity on C26 cells. So, SN38/Exo-Apt could be considered as a great platform for the therapy of colorectal cancer.

Keywords: Cancer, Exosomes, Human mesenchymal stem cells, Aptamer,, SN38

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Techniques Involved Recombinant DNA And Genetics (Review)

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Introduction: Recombinant DNA technology involves modifying genetic material outside of an organism to achieve improved and desired properties in the organism or as a product. It also includes procedures for analyzing or combining DNA fragments from one or more organisms, including the introduction of ribonucleic acid (rDNA) molecules. It replicates in the cell or integrates into the genome of the target cell. Recombinant DNA technology has many applications in fields as diverse as agriculture, public health, gene therapy, environmental science and pollution research, clinical pharmacy, and hormone and vaccine development. The main point of inquiry in this field is to tentatively investigate the conceivable outcomes of repairing harmed human DNA, mending or improving future human bodies. The purpose of this article is to provide an overview of the available molecular genetic methods and their capabilities and to provide insights into their application to neuroscientific problems.

Methods: The purpose of this article is to describe the tools of recombinant DNA technology and their use for cloning and manipulating DNA constructs. We will first discuss methods for isolating DNA fragments from the genome and other DNA vectors. We then describe molecular cloning: how these isolated fragments are inserted into storage vectors and mass-produced using bacteria. We then describe how DNA fragments or recombinant DNA constructs are purified from other DNA molecules. Finally, we describe the methods for reading the molecular sequence of a DNA construct. After creating and purifying a new DNA construct, a scientist can introduce the construct into different cells or use it to create a genetically altered organism . Intact DNA only occurs in living cells or resting forms (e.g. bacterial spores). As soon as a cell dies, repair of existing damage stops, and enzymatic degradation begins. This means that the acquisition of new genes, such as antibiotic resistance genes from animal feed, is – most likely – a vanishingly rare phenomenon. Furthermore, the simple transfer, integration, and expression of genes is not enough for the spread of genes, rather it is the selection pressure that drives the spread of genes in a particular environment. Once a bacterium acquires a functional gene that confers antibiotic resistance and selective pressure is applied, usually through the therapeutic use of the drug, it is likely that this functional gene will spread and accumulate in the

resulting population. Recombinant rDNA technology involves methods of analyzing or combining DNA fragments from one or more organisms , including introducing an rDNA molecule into a cell for replication or integration into the target cell's genome. Advances in molecular biology in the early 1970s, including success in producing and delivering DNA molecules into cells, revolutionized both science and industry. The first genetically modified organisms were bacteria that produced simple proteins of pharmaceutical importance, such as insulin. The development of recombinant DNA technology (also called genetic cloning of gene splicing), a method by which DNA from different biological sources is combined to determine its sequence or manipulate its expression, ushered in and ushered in the era of genetic discovery to the industry. In short, the seven main steps of recombinant DNA technology are: 1) isolation of the DNA 2) cutting the DNA at specific locations 3) isolation of the desired DNA fragment 4) amplification of the gene of interest by PCR 5) binding. Isolation of DNA fragments in vectors 6) Introduction of recombinant DNA into host cells/organisms 7) Production or cultivation of foreign products. Recombinant DNA (rDNA) technology has enabled a breakthrough in plant and animal biotechnology. The power of rDNA technology relies on our ability to study and change the function of genes by manipulating and transforming them in plant and animal cells. To achieve this goal, various molecular biology tools are used, including DNA isolation and analysis, molecular cloning, quantification of gene expression, determination of gene copy number, transformation of a suitable host for replication or transfer to crop plants, and analysis of transgenic samples. Installations. In 1982, British geneticist Alex Jeffreys studied small repetitive DNA, a class of DNA sequences that do not encode proteins. By comparing the gel electrophoresis patterns of these DNAs in different people, he made the extraordinary observation that they appeared to be unique to each person. He realized that this would make molecular “fingerprints” much less clear than traditional fingerprints, which have been a mainstay of forensic science for decades. The technique developed was called DNA profiling, also known as DNA fingerprinting or DNA typing. Recently, research on recombinant DNA technology has dominated the biological sciences. This reframes biological problems and possible solutions so that scenarios involving editing the genome and creating a new virus, chromosome, or genetic variant are now commonplace in laboratories. The power of recombinant DNA technology is actually threefold: first, we can completely break down a complex mixture of biological molecules into its individual components; Secondly, we can obtain an unlimited amount of the molecule of interest, and third, we can translate an experimental problem from protein chemistry into the language of nucleic acids, thereby gaining access to a range of experimental techniques including rapid structure destruction primary methods through sequence analysis from nucleotides. For these reasons, recombinant DNA technology has had a

profound impact on modern biology, making it possible for the first time to study the molecular genetics of complex eukaryotic systems. As the articles in this issue demonstrate, the potential of these approaches is now also making itself felt in the field of neuroscience. The purpose of this article is to provide an overview of the available molecular genetic methods and their capabilities and to provide insights into their application to neuroscientific problems. Strategies for molecular cloning Each strategy involves two essential elements: the production of cDNA clones from mRNA and the selection of clones of interest. However, for low-abundance mRNA molecules (0.1% or less of total mRNA), purification is much more difficult, and various strategies have been developed for this purpose. For example, using synthetic oligonucleotides, suitable clones are selected from an “eDNA library,” a collection of clones that come from the entire mRNA population of the tissue. Between these extremes, there are many possible combinations of partial mRNA purification and clonal selection. A good example of such a combined strategy is the recent isolation of tyrosine hydroxylase cDNA clone. Northern Blot can also be used to detect mature cytoplasmic mRNA precursors in nuclear RNA preparations: these appear as less intense and larger bands. However, for many purposes, gel fractionation is not important because hybridization of the labeled probe with mRNA samples bound directly to nitrocellulose (“dot blot”) measures mRNA abundance. Alternatively, the hybridization of DNA or RNA in solution to form a labeled probe allows for a more precise measurement of the abundance of a particular sequence. Each of these techniques can be used to measure changes in the steady-state concentration of cytoplasmic expression of a particular mRNA after disruption, damage, or medical treatment Finally, The cDNA clone can be used to define the structure of the gene encoding the cloned mRNA. A fragment of genomic DNA containing the corresponding gene can be visualized using the Southern blot method. This is the precursor to the Northern blot method. In the Southern blot method, genomic DNA is digested with a restriction enzyme, the fragments are separated by agarose gel electrophoresis and transferred to nitrocellulose. Hybridization with a labeled eDNA clone allows the detection of fragments with complementary sequences: in the case of a single-copy gene, only one or two bands are free; A count of more than bands may indicate a family of related genes. For gene isolation, a library of genomic clones is usually screened. The present and the future In the past five years, recombinant DNA techniques have been directly responsible for several important advances in biology, most notably the discovery of intron-exon gene structure and DNA rearrangements in genes encoding immunoglobulins. However, the impact of this technology on neuroscience has been far less comprehensive and largely limited to the characterization of neuropil progenitors. Theoretically, it is possible to obtain an eDNA clone corresponding to any protein, provided that a suitable mRNA source is

available and the appropriate clone can be chosen. In practice, the main problems are in the selection of the clones, especially when there is no suitable assay for the protein in question. Another approach to identifying new proteins in the brain is to select eDNA clones from rat brain mRNAs That are expressed in the brain but not in other tissues. In addition to isolating several clones of novel brain proteins, which are currently the subject of intensive research, this strategy led to the identification of a common nucleotide sequence that could act as a marker for brain-specific ~L genesecombinant DNA Formation And Application Recombinant DNA is completed by three different methods: transformation, introduction of a phage, mainly lambda phage, and non bacterial transformation, namely gene gun or microinjection. With recombinant DNA technology, cloning not only allows you to recombine a piece of DNA to encode a specific gene but also manipulate genes to change their regulatory sequence. The coding region can be placed under the control of a promoter and introduced into an expression system, which may be a virus or a bacterium, to observe regulatory changes. Coding regions of recombinant DNA produce proteins with unique properties.The insert has a selectable indicator that allows the identification of recombinant molecules. In a host cell, in which the newly introduced gene dies under the influence of the antibiotic supplied, a host with a vector is found. The vector is inserted into the host cell in a process called transformation. Plasmids are generally used to deliver the gene of interest as a vector, and the methods for isolating them vary depending on the host organism. Based on the phenotypic effect of genes and their location in the chromosome, genes are further divided into subgroups such as simple operons, complex operons, gene regulons, and multiple regulons. Ligation Two types of vectors are used in recombinant DNA research: circular particles such as plasmids and cosmids and linear cloning vectors such as those derived from the bacteriophage lambda. In both cases, to connect the vector to the target DNA fragment, it is first cut with a restriction enzyme that creates ends that are compatible with the ends of the target. Therefore, circular vectors are converted into a linear form before binding to the target. The inserted fragment is then ligated into the prepared vector to create a recombinant molecule that can replicate once introduced into the host cell. The ability of two DNA molecules to join depends on the concentration of their ends; The greater the concentration of compatible ends (those that can be joined), the greater the likelihood that the two ends will meet and be joined. The degree of circulation that occurs in a ligation reaction depends on the concentration of ends of the same molecule that are close enough together to potentially and effectively interact. For any DNA fragment, the concentration depends on the length of the fragment and not on its concentration in the ligation reaction. Packaging of recombinant genomes After ligation of the inserted fragment with the λ arms of the vector and concatemerization of the recombinant λ genomes, the DNA must be

encapsulated into the head and tail structures of the phage proteins so that they are fully capable of infecting susceptible cells. coli. This is achieved by adding bound recombinant λ-DNA to a prepared extract containing the enzymatic and structural proteins required for the complete assembly of mature viral particles. The packing mixture is then inoculated with host cells, which allow the formation of plaques on agar plates. Measuring the efficiency of these reactions is called packing efficiency. Transformation Efficiency After binding the DNA fragment to the plasmid vector, the recombinant molecule must be introduced into the host bacteria where it can replicate in a process called transformation. The plasmids used for cloning contain an antibiotic resistance gene that allows the selection of transformed cells. Transformation efficiency is a quantitative measure of the number of cells occupying the plasmid. Applications of Recombinant DNA Technology Health and Diseases. Recombinant DNA technology has a wide range of applications in treating diseases and improving health. The following sections describe important advances in recombinant DNA technology aimed at improving human health Gene Therapy: Gene therapy is an advanced technique with therapeutic potential in healthcare. The first successful report in the field of gene therapy to treat genetic diseases has provided a safer direction for treating the deadliest genetic diseases. The main strategies that are used now include vaccination with tumor cells engineered to express immunostimulatory molecules, vaccination with recombinant viral vectors encoding tumor antigens, and vaccination with host cells engineered to express tumor antigens It is preferable to add a functional gene rather than a single protein because proteins are rapidly degraded while a properly integrated gene continues to be expressed. It has been proven that gene therapy is a complex process that includes several phases and consists of the production of a vector carrying a specific gene and its introduction into the cell. Once the vector has introduced the transgene into the cell, the gene must pass through the cytoplasm and enter the nucleus. The transgene located in the cell nucleus must be stably integrated into the genome: only integrated copies of the gene can be consistently replicated during each genome replication. Finally, appropriate and regulated expression of the transgene must be achieved, which is not a trivial task since most vectors insert the gene they carry at random positions. In the case of accidental insertion, two problems arise: (i) In most cases the gene is in a chromosomal environment that does not allow its transcription; and (ii) the gene may be found in other genes or their regulatory sequences, leading to the inactivation of these host genes, some of which may be essential. To overcome these problems, existing methods are constantly being improved or completely new approaches are being created. Alternatively, therapeutic DNA can be delivered directly into target cells. Another option is to use liposomes, artificial lipid spheres with a watery core that contains DNA. Another approach involves chemically linking

DNA to molecules that can bind to specific receptors on the cell surface or facilitate nuclear transfer. Among nonviral vectors, artificial human chromosomes dominate with virtually unlimited gene expression capacity, stability, and lack of immunogenicity EPILOGUE Recombinant DNA techniques developed by molecular biologists over the past few decades have had far-reaching consequences in fields as diverse as forensics, medicine, and agriculture. This has given rise to many high-tech industries. Like many scientific breakthroughs that have changed our lives, research that began in the ivory towers has reached the mainstream. Recent advances in recombinant DNA technology C) Currently, research is focused on the development of subunit vaccines that contain the most potent immunogenic antigens of a given pathogen. Recombinant viruses have several interesting properties that make them extremely effective in triggering a T cell-mediated immune response. Recently, this cell-mediated immunity was shown to be essential for protection against malaria and AIDS because it contains the most immunogenic virus ever. given pathogen. Recombinant viruses have several interesting properties that make them extremely effective in triggering a T cell-mediated immune response. Cell-mediated immunity has recently been shown to be essential for protection against malaria and AIDS. D) A new molecular biology tool has recently been developed through the development of baculovirus surface imaging, using various strategies to display foreign peptides and proteins on the surface of budding virions. This eukaryotic display system allows large, complex proteins to be displayed on the surface of baculovirus particles, making it a versatile system in molecular biology. F) Mites have been shown to be important. Sources of household allergens linked to asthma and other allergic diseases. Recombinant DNA technology, together with other immunological and molecular biology techniques, has contributed significantly to a better understanding of the biology of house dust mites and their role in allergic diseases. G) Recombinant DNA technology has enabled the development of molecular cloning vectors that enable the expression of heterologous genes in a variety of animal viruses. A virus that encodes the bacteriophage T7 RNA polymerase is used as the expression vector system. The selected gene is inserted into a plasmid vector intended for gene expression under the control of the T7 promoter J) The complement system is an important element of defense against foreign organisms and functions in both the innate and adaptive immune systems. C4b binding protein (C4BP) is a potent circulating soluble inhibitor of the classical complement and lectin pathways. In recent years, the relationships between the structure and functions of C4BP have been elucidated by combining computational molecular analysis and recombinant DNA technology BIOMEDICAL SIGNIFICANCE It is useful in providing a clear picture of the molecular basis of many diseases. With this technology it is possible to produce large quantities of human proteins used in Therapy such as Use of

proteins for vaccines (e.g. against hepatitis B) and for diagnosis. This technology is used to diagnose existing diseases and predict their risk Development of a particular disease. Food and Drug Administration. Agriculture Since golden rice is a fortified source of vitamin A and is used in the production of medically important agricultural products, such as the production of human growth hormone and edible vaccinesHigh-quality crops are obtained by crossing different varieties by inserting a new gene from other suitable varieties or a wild relative. Nanobiotechnology Nanobiotechnology can create atomic or molecular machines by incorporating them into biological systems, which is why it is considered a combination of biotechnology and nanotechnology. Nanobiotechnology also has applications in clinical sciences such as disease diagnosis, drug delivery, and molecular imaging Medical Genetic probes are used to diagnose the disease at an early stage and determine the likelihood of its occurrence in future generations .Recombinant DNA technology also helps humanity cure many diseases that may be difficult or impossible to cure. Many recombinant proteins synthesized through DNA manipulation are currently used to treat diseases. Protein engineering has been used to develop second-generation variants with improved pharmacokinetics, structure, potency, and bioavailability. For example, in neutral solutions used for treatment, insulin is often in the form of zinc-containing hexamers. However, absorption is limited by this self-association. By developing unique amino acid replacements, molecular biologists are now able to produce essentially monomeric insulin at therapeutic concentrations. It turned out that this insulin is not only able to maintain its biological effect but is also absorbed two to three times more effectively. Role of Biotechnology in Animal Sciences Animal biotechnology deals with genetically engineering animals through the application of molecular biology techniques, it is also used to synthesize several proteins that are beneficial for the improvement of growth and treatment of animals as well as humans. Transgenic animals are produced by inserting the desired gene of interest in them. The gene of interest injected into a cell is done using different techniques like retroviruses-mediated, pronuclear micro-propagation; sperm-mediated transfer, and embryonic stem cell methods. Molecular biology and recombinant DNA technology have revolutionized the field of toxicology. such technology provides a means to manipulate molecules critical to these processes and an opportunity to examine the effects of these manipulations in living systems and to elucidate the physiological roles of the protein under investigation. KEY PRINCIPLES RECOMMENDATIONS Although our assessments of the risks associated with each line of research into recombinant DNA molecules may vary, few, if any, believe that this methodology is risk-free. Valid principles to address this potential risk are: (i) isolation should be considered in the experimental design and (ii) the effectiveness of isolation should correspond as closely as possible to the estimated risk.

Results: The recombinant DNA technology has a significant impact on improving the quality of human life. It has several applications in different facets of human life. The most important output of this technology is developing human insulin which saves millions of humans around the world. It is often used to treat diseases and improve health. This review describes important advances in recombinant DNA technology that aim to improve the applications of recombinant DNA technology in human medicine, the food industry, and agriculture.

Conclusion: Recombinant DNA technology is a revolution in biotechnology, contributing to the development of new drugs, hormones, enzymes, and treatments for many health, agricultural, and environmental problems. Genetic engineering involves recombinant DNA in which a selected gene can be cloned and/or manipulated. These cloned genes are records of the functions, nature, enzymes, or hormones of the human body. It can be performed using state-of-art technologies and tools that can be applied either in vitro or in vivo. In this review paper, this emerging technology has been reviewed based on available literature to increase the knowledge about this evolutionary technology which will drive human civilization to an advanced level

Keywords: Recombinant DNA, Genetic Engineering, Biotechnology, Molecular Cloning

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Telenursing: A step for care management in disaster and emergencies (Research Paper)

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Introduction: Unusual impacts of disasters on normal living conditions pose challenges to the health system. Nurses who take care of disaster victims may face situations that make decision-making difficult; hereon, the use of new technologies can be a useful solution. The study aimed to identify the telenursing care during incidents and disasters.

Methods: The study was conducted at a medical science university in Iran from 2018 to 2019. This was a semi-structured interview-based qualitative study using content analysis. Eighteen nurses, nursing teachers, and emergency medical technicians were included in the study. Data analysis was performed using inductive content analysis and coding with MAXQDA (2010) software. The Lincoln and Guba (1985) trustworthiness criteria were used for the reliability and validity of the data.

Results: Telenursing in critical and supportive care was the main theme identified from data analysis. This theme included six main categories: (1) management of trauma, (2) technical skills, (3) care and decision-making in stressful situations, (4) management of patients with special needs, (5) life-saving intervention, and (6) psychological and emotional supports.

Conclusion: Telenursing in disasters is the turning point of the care management of victims. In order to achieve this goal, nurses should acquire the relevant knowledge, skills, and abilities.

Keywords: Disasters, incidents, qualitative study, telenursing.

The Anti-Inflammatory Effects of the Nutrition Bio-Shield (NBS) Supplement Intake on Adjuvant-Induced Rheumatoid Arthritis in Rat (Research Paper)

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Introduction: In rheumatoid arthritis (RA), the autoimmune response against articular tissues is the first mechanism proposed for the pathogenesis of the disease (1). It has been suggested that genetic and environmental factors could develop the disease (2,3). Environmental factors including infections, diet, and lifestyle may activate the genetic drivers of RA to stimulate the innate and adaptive arms of the immune system in order to produce inflammatory mediators namely tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), and IL-6 (4). It has been declared that while environmental factors could propel innate immune cells to the articular space, genetic abnormalities affect T-lymphocytes repertoire selection and antigen presentation, which could shift the balance between the osteoblasts and osteoclasts, leading to bone erosion and joint deformity (5). These two important symptoms influence a patient's quality of life (5). The results of previous study revealed that the prevalence of depressive symptoms and anxiety resulting from physical disability was high in RA patients, which could, in turn, influence their social lives (6). Although numerous decades have passed since the first description of RA and a progress has been made in the understanding of the disease pathogenesis, the diagnosis of this complication and the treatment strategies for the patients have not run into any changes. Nutrition bio-shield (NBS) supplement is a herbal dietary supplement derived from wheat grains (NBS Organic Company, Turkey). It has been stated that the wheat germ contains considerable amounts of tocopherol, policosanol, phytosterol, riboflavin, thiamin, and niacin (7). Furthermore, in another study, it was found that the NBS supplement was able to stimulate the immune system upon changing the balance of neutrophils to lymphocytes (8). Since 2010, the European League Against Rheumatism and the American College of Rheumatology have elected rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) for serological diagnosis of RA (9). By making some modifications to the treatment, the treatment of this diseases begins shortly after its detection; to this end, immunosuppressive agents like non-steroidal antiinflammatory drugs and glucocorticoids are used (10). Recently, TNF

blockers have found their way into the treatment protocol of RA, as either a single agent or in combination with immunosuppressive drugs. Despite their impressive success, several side effects, like the high risk of infections, have restricted the clinical usage of such agents in RA patients (11). IL-6 inhibitors, rituximab, and abatacept (T cell inhibitor) are other therapeutic agents that have been under evaluation in pre-clinical studies (12). In addition to these synthetic drugs, herbal and natural medicines also consist a fertile ground for treating RA (13,14). Since many of these therapies have proven efficient in ameliorating the disease symptoms without serious toxicity, much attention has been drawn to this field so far. The current study attempts to assess the NBS supplement's therapeutic potential in the case of RA-induced rats.

Methods: Animal and Ethical Statements Twenty-five male Wistar rats with the estimated weights of 200-250 g were purchased from Institute of Medicinal Plants, ACECR, Karaj, Iran. They were kept in special cages at 22-25o C and provided with food and water in 12 hours of light and darkness. They were transferred to the laboratory one week before the experiment to adapt them to the new conditions. The protocol was investigated and confirmed by the Institutional Review Board of Islamic Azad University of Mashhad (IR.IAU.MSHD.REC.1398.233). Induction of Rheumatoid Arthritis (RA) in Rats To induce the RA model, rats received xylazine ketamine for anesthesia and then, 0.2 cc Freud's complete adjuvant (FCA) was injected into their knees (15). It should be noted that one group of animals consisting of 5 rats was only injected with 10 mg of normal saline and it remained as the control group. RA-induced rats were then divided into four groups (each having five rats) for further analysis. Treatment of RA-Induced Rats with the NBS Supplement In order to measure the therapeutic value of the supplement, three groups of RA-induced rats received oral treatment containing different NBS supplement concentrations (12.5, 25, and 50 mg/kg) in the form of gavage for 30 days after induction of RA. The ingredients of the NBS supplement are shown in Table 1. After 30 days, xylazine ketamine was used to anesthetize the rats and 3-5 mL of blood was sampled from their hearts to assess the serum levels of ESR using the Westergren method (16), CRP, and RF (each evaluated three times to ensure the results are exact). Of note, one of the rat groups did not receive any supplement concentrations and was considered as the negative control. Statistical Analysis The serological tests were performed in triplicate and the outcome was yielded in the form of the mean ± standard deviation. In addition, the KolmogorovSmirnov test was adopted to confirm the normality of data distribution. The One-Way ANOVA test via IBMSPSS software was also employed to gauge the data significance with a favorable probability level of $p<0.05$. The Tukey Post-hoc test was used to perform Post-hoc analysis with One-Way ANOVA

Results: To evaluate whether the application of the NBSsupplement treatment to RA-induced rats could ameliorate the inflammatory responses, we first evolved an RA model in rats by injecting FCA into their knees. Analysis of their blood samples revealed that the number of inflammatory parameters such as ESR, CRP, and RF increased in the RA-induced rats in comparison to the control group (FCA-untreated rats) (Table 2). Then, RA-induced rats were treated by the NBS supplement (12.5, 25, and 50 mg/kg) for a month. Our results demonstrated that the NBS supplement could not only robustly diminish the levels of ESR and CRP, but also significantly reduce the levels of RF in the treated rats (Table 2). Although the ESR and CRP levels of rats in group 1 (treated with 12.5 mg/kg of the NBS) reduced in comparison with the negative control group, they remained higher than normal (Figure 1). Maximum effect was observed in the group treated by the 50 mg/kg NBS supplement. The conducted ANOVA test results point to a statistically significant difference among ESR, CRP, and RF levels of groups [(ESR: $F(4.20)=88.92$, p-value=0.00), (CRP: $F(4.20)=121.88$, p-value=0.00), (RF: $F(4.20)=147.71$, p-value=0.000]. ESR, CRP, and RF of RA-induced mice were statistically significantly lower after treatment by any dosage of the NBS supplement compared to the negative control (untreated) group. Mean ESR in group 3 was statistically considerably lower than that in groups 1 and 2 ($p<0.001$ and $p=0.002$, respectively). However, no statistically significant difference was found between group 1 (12.5 mg/kg of the NBS) and group 2 (25 mg/kg of the NBS) ($p=0.172$). The mean CRP in groups 2 and 3 was statistically and significantly lower than that in group 1 ($p=0.001$ and $p=0.003$, respectively). No statistically significant difference was found between group 2 (25 mg/kg of the NBS) and group 3 (50 mg/kg of the NBS) ($p=0.997$). Finally, RF level was statistically significantly lower in group 3 than that in groups 1 and 2 ($p<0.001$ and $p=0.001$, respectively). However, no noticeable difference between groups 1 and 2 was observed ($p=0.279$). All results of the ANOVA and the Tukey Post-hoc tests are shown in Table 3.

Conclusion: In light of obtained findings and based on their interpretation, this study proposed NBS supplement as an herbal dietary supplement that could restore the blood RF of the studied rats to a normal level at any applied dosages. In addition, the supplement had significant restoring effect on the ESR and CRP levels at higher concentrations, especially at 50 mg/kg. To reduce both inflammatory markers and RF, the administration of 50 mg/kg of the NBS supplement managed to produce better anti-inflammatory outcome, meaning that it could be integrated into the treatment protocol of RA. Yet, further analysis is required to investigate its therapeutic potential. For future research, it is suggested that more clinical and histopathological data before and after the intervention of the NBS may open up a new frontier to ensure a better understanding of its therapeutic effects on the RA disease.

Keywords: Rheumatoid arthritis, nutrition bio-shield supplement, anti-inflammatory agents

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The apoptotic effects of myricetin on Breast Cancer Cells by induction of extrinsic and intrinsic apoptotic pathways (Research Paper)

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Introduction: Myricetin is a polyphenol flavonoid with nutraceutical values which is abundantly found as the main ingredient of various foods and beverages. It has been reported that the function of myricetin is to trigger apoptosis in several types of cancers. The present study intended to investigate the apoptotic effects of myricetin on MCF-7 breast cancer cells and to assess its possible mechanisms of action.

Methods: MCF-7 breast cancer cells were assigned to four groups: Control (cells in normal condition); myricetin (cells treated with the IC50 dosage of myricetin) in three different incubation times (24, 48, and 72 h). The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, annexin V assay, flow cytometry, real-time polymerase chain reaction (PCR), and caspase-3 assay were used to estimate the apoptosis function of myricetin in breast cancer.

Results: The expression levels of apoptosis-related genes caspase-3, caspase-8, caspase-9, and the BAX /Bcl-2 ratio as well as the expression of p53, BRCA1, GADD45 genes were significantly increased following the treatment of MCF-7 breast cancer cells with myricetin. The annexin V assay demonstrated the significant expression of annexin which was also detected by flow cytometry.

Conclusion: Myricetin efficiently induces apoptosis in MCF-7 breast cancer cells by evoking both extrinsic and intrinsic apoptotic pathways. Myricetin may exert its apoptotic effects on MCF-7 cells by inducing the BRCA1- GADD45 pathway.

Keywords: Myricetin- flavonoid- MCF-7- apoptosis

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The Application of Artificial Intelligence in Early Detection of Esophageal Cancer: A Comprehensive literature review (Review)

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Introduction: Esophageal cancer is the eighth most common cancer in the world and the sixth leading cause of cancer mortality. This malignancy mainly consists of two types: adenocarcinoma and squamous cell carcinoma. Most esophageal cancer patients in Western countries have adenocarcinoma, unfortunately with a five-year survival rate of less than 20%. Despite the increasing incidence of adenocarcinoma, squamous cell carcinoma is the most common type of esophageal cancer in the world, with a three-year survival rate of only about 20%. This is mainly due to late diagnosis of the disease, as more than 40% of patients are diagnosed only when metastasis has occurred. Endoscopy and biopsy with pathological examination are the basis for diagnosing esophageal cancer, but this modality is invasive, time-consuming, expensive, and highly dependent on the individual's accuracy. Therefore, our need to identify efficient diagnostic modalities has led to widespread use of artificial intelligence (AI) in early detection of this disease. Therefore, the aim of this study is to evaluate the simultaneous use of AI for endoscopic diagnosis, pathological diagnosis, and identification of relevant genes associated with esophageal cancer.

Methods: In this review study, a comprehensive search was first conducted in the PubMed, Web of Science, Scopus and Google Scholar databases. After removing duplicate and non-English articles, article abstracts were reviewed to determine their relevance to the evaluated subject. After removing irrelevant articles, the full text of the articles was examined. Their data was extracted and combined and compared with each other to achieve the final result.

Results: Machine Learning (ML) and Deep Learning (DL) algorithms have been highly regarded for creating efficient diagnosis models. The application of artificial intelligence in early detection of esophageal cancer is well established in three main areas: endoscopic-based diagnosis, pathologic-based diagnosis, and identification of related genes. The application of Supervised ML algorithms along with Narrow Band Imaging (NBI) and High-Definition White-Light Endoscopy (HD-WLE) can improve the diagnostic accuracy of existing modalities in detecting Barrett esophagus. The use of

these modalities along with DL algorithms can not only increase diagnostic accuracy but also determine the location of lesions for biopsy. application of HD-WLE images with DL algorithms can also increase the diagnostic accuracy of esophageal cancer, especially in young endoscopists and mid-level practitioners. How ever, different results have been reported regarding the application of AI in Endoscopic Optical Coherence Tomography and classification of Intrapapillary Capillary Loops. The use of artificial intelligence models for pathological classification of esophageal cancer in terms of No Dysplasia, Low Grade Dysplasia, and High Grade Dysplasia has increased the accuracy of this gold standard diagnosis method. and eventually DL models and Conventional Neural Network (CNN) can be useful in early detection of cancer by identifying microRNAs, long non-coding RNAs, and cancer related protein markers.

Conclusion: Nowadays, the use of artificial intelligence models in the detection of endoscopic, pathological, and gene-based esophageal cancer is expanding. Many studies accompany the application of these algorithms with daily modalities to increase the diagnostic accuracy of the disease in the early stages. Conducting further studies with appropriate input and training data volume and effective validity methods can identify more dimensions of this issue and pave the way for the wider application of these algorithms in early detection of esophageal cancer.

Keywords: Artificial Intelligence, Esophageal cancer, diagnosis, Barrett esophagus

The Application of Gene Editing Technologies in Regenerative Medicine (Review)

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Introduction: Gene therapy is an innovative approach in precision medicine in which, by editing genome data, specialists could overcome medical deficits. On the other hand, regenerative medicine is a revolutionary branch of science that uses cells, scaffolds, and growth factors to make permanent fundamental changes in health. Application of viral or non-viral vector-based gene therapy and CRISPR/Cas system as a powerful and accurate gene tool in cooperation with tissue engineering methods such as cell therapy may be a logical perspective to coping with diseases.

Methods: This review was prepared by searching Science Direct, Google Scholar, Pub-Med, Scopus, and Web of Science databases.

Results: One of the primary applications of gene editing in tissue engineering is enhancing cellular properties. Researchers can create cells with improved regenerative capabilities by precisely altering genes related to cell proliferation, differentiation, and survival. For instance, editing the genes of mesenchymal stem cells can enhance their differentiation into specific cell types, such as osteoblasts or chondrocytes, for bone and cartilage tissue engineering. This approach accelerates tissue growth and improves the overall success of engineered constructs. Gene editing also plays a pivotal role in addressing the immunological challenges associated with tissue transplantation. By modifying donor cells to reduce their immunogenicity, tissues engineered using gene-edited cells are less likely to trigger immune

responses upon transplantation. This opens new avenues for personalized tissue engineering, as it mitigates the need for extensive immunosuppressive therapies and broadens the donor pool. Furthermore, gene editing enables the creation of disease-specific models for drug testing and disease research. Engineered tissues with genetic mutations associated with various diseases, such as cancer or genetic disorders, provide invaluable platforms for studying disease mechanisms and screening potential therapeutic interventions. This approach accelerates drug development and fosters a better understanding of disease pathophysiology. In addition to enhancing cellular properties, gene editing can incorporate specific functionalities into engineered tissues. Researchers can introduce genes encoding for growth factors or other bioactive molecules to promote tissue vascularization, innervation, or self-repair mechanisms. This approach is particularly promising for complex tissues like the heart or the nervous system, where mimicking native tissue functionality is essential for successful transplantation. Another compelling application is the development of bioartificial organs and organoids. Gene editing enables the creation of scaffolds populated with cells that closely resemble native tissues, facilitating the generation of functional organs for transplantation. Similarly, it allows the refinement of organoids for disease modeling and drug testing, bringing us closer to personalized medicine approaches. Despite the remarkable progress in gene editing for tissue engineering, ethical and safety concerns persist, necessitating rigorous oversight and continuous research into the long-term effects of genetically modified tissues.

Conclusion: Gene editing applications in tissue engineering hold great promise in revolutionizing regenerative medicine, personalized therapies, and disease research. As technology advances and our understanding of genetic manipulation deepens, we can anticipate even more innovative and transformative breakthroughs in tissue engineering, offering hope for millions of patients awaiting life-saving treatments and organ transplants.

Keywords: Gene therapy, tissue engineering

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The Application of Gene Expression Analysis by ART in the Selection of Competent Genes for Pregnancy Prediction (Research Paper)

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Introduction: One of the most important steps in human assisted reproductive technology (ART) is selecting high-quality embryos for transfer to ensure successful outcomes. Traditionally, assessment of physical characteristics of the oocyte and embryo famed as morphological measures were reliable but it cannot fully determine the developmental potential of an embryo. To bypass limitations, biological measures such as gene expression profiles of cumulus cells (CCs) to enhance the accuracy of embryo selection were developed. It is possible to gain insights into the embryo's pregnancy potential by analyzing the gene expression patterns of these cells which surround the oocyte. Among of diseases that can deteriorate fertility, polycystic ovary syndrome (PCOS) affects the ovary's function, hormonal balance, and can alter the gene expression profile of CCs leading to irregular ovulation and potential difficulties in conceiving. Studies have shown some specific genes (e.g., CALM, PSMD6, and AK124742) are suggested for predicting pregnancy and were differentially expressed in the CCs of pregnant patients compared to the non-pregnant group and in PCOS and non-PCOS ovaries. This study was designed to explore the candidate genes for the selection of the most viable embryo.

Methods: Cross-sectional and 3-week prospective study was conducted between April 2020 and January 2021 at Hazrat Maryam Fertility Center of Shahid Beheshti hospital. This study investigated associations of infertility with gene expression among middle-aged Iranian adults with an average age of 32.48 years. Over all 66 patients (33 in the control group and 33 in the PCOS Group) participated who underwent an In vitro fertilization (IVF) or Intracytoplasmic sperm injection (ICSI) treatment participated. In normal ICSI or IVF cycles, a part of the CCs separated from the cumulus-oocyte using two sharp needles and were rapidly transferred into a tube containing a free enzyme medium. All of the collected CCs were washed with PBS and after centrifugation at 12,000 g for 2 minutes, The CCs mass of each patient was quickly stored in a -80 ° C freezer for Real-time PCR assessment of CALM, PSMD6, and AK124742. Glyceraldehydes-3- phosphate dehydrogenase

(GAPDH) was used as an endogenous control. The expression level of each target gene was calculated as 2−ΔΔCt. Statistical analysis was performed using SPSS 20.00 Quantitative variables using mean and standard deviation (SD). The results were analyzed by the independent sample t-test and One-way ANOVA. The nominal and frequency data were analyzed using Chi-square test or Fisher's exact test as appropriate. The Pearson correlation coefficient was used to examine the parametric variables (for nonparametric variables, Spearman's correlation coefficient was used). P values less than 0.05 were considered statistically significant for all the statistical tests.

Results: Expression of CALM1, PSMD6, and AK124742 revealed differential regulation in the pregnant group and the non-pregnant group. CALM1 showed a modest upregulation in the pregnant group, this increase did not reach statistical significance. In contrast, PSMD6 ($p < 0.001$) and AK124742 ($p < 0.05$) demonstrated significantly higher expression levels in pregnant compared to non-pregnant. The expression of CALM1 and AK124742 genes increased significantly and the expression of PSMD6 significantly downregulated in PCOS group compared to the control group ($p < 0.05$).

Conclusion: These three specific genes in CCs have crucial role in pregnancy. PSMD6 can encode a regulatory subunit of the proteasome which degrades intracellular proteins and its activity may be increased to handle changing demands on protein metabolism in pregnant women. Though the function of AK124742 is unknown, its significant upregulation points to a potential role during pregnancy which needs further investigation. CALM1 encodes calmodulin for essential calcium signaling in ovulation and uterine contraction. Its upregulation could reflect perturbations in calcium signaling contributing to the infertility associated with PCOS. The different regulation of AK124742 and PSMD6 in pregnancy and PCOS provides evidence that PCOS specifically disrupts the gene regulatory networks induced during normal pregnancy. It is suggested that selecting genes that affect the reproductive process without careful examination of the path of the effect of these genes and only relying on comparing the expression of these genes in fertile and infertile groups cannot be an accurate method for selecting these genes.

Keywords: AK124742, CALM1, PSMD6, Granulosa cells, PCOs

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The Application of Taurine in Wound Healing (Review)

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Introduction: The drug delivery system enables the release of the active pharmaceutical component to achieve an efficient programmed response. Taurine is a free amino acid that plays an important role in some main biological processes and has the potential to be encapsulated and delivered to specific tissues or cells involved in angiogenesis for tissue engineering approaches. One of the major paths in wound healing is preparing conditions that help angiogenesis.

Methods: An electronic search was done in the PubMed, Scopus, and Google Scholar databases from January 2016 to September 2023 with the keywords taurine, tissue engineering, and wound healing. A combination of keywords was done using Boolean drivers AND and OR, and then the data analysis was done precisely.

Results: It is adopted that taurine has some antioxidant and anti-inflammatory properties, which can indirectly support angiogenesis, and there is limited research on its direct effects on blood vessel formation. Taurine could have beneficial effects in various conditions. Additionally, recent studies showed that taurine plays a vital role in the aging process, even though by reducing histamine level degranulation of the mast cells

Conclusion: Finally, by a glimpse, it is known that taurine may have the potential to be used in bioprinting, the ability to be encapsulated in a nanocarrier, and cell therapy in tissue engineering. Despite proven facts about the drug delivery system and taurine separately, It is necessary to do more research to find challenges and solutions. On the one hand, whether taurine

can be used directly on wounds or not, and on the other hand, strong in vitro or in vivo studies should be designed and carried out.

Keywords: taurine, tissue engineering, and wound healing

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The aspects of hematological factors among COVID-19 patients affected to yeast infections (Research Paper)

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Introduction: since the COVID-19, it causes many hospitalization and deaths, especially in immunocompromised patients. Yeast infections occur most commonly as a secondary infection in immunocompromised individuals. However, the diagnosis of fungal infections is controversial,. Hematologic parameters in COVID-19 patients affected by yeast infections can predict prognosis and may help patient treatment. The aim of this study is to investigate the hamatological parameters in COVID-19 patients associated with yeast infections.

Methods: 1531 COVID-19 patients were examined . Hematological factors such as platelets, White blood cells and D-dimer evaluated for any yeast infections. All data were analyzed by IBM SPSS statistics 22 software, and for comparison between two groups, student's t-tests were used.

Results: The average age of patients was 60.37% years, of which (47.9%) 732 were female and (52.1%) 796 were male. Among the 1531 COVID-19 patients ,227 (14.8%) showed yeast infections. hematological factors showed a significant relationship between two groups of COVID-19 patients and COVID-19 patients with yeast infections.

Conclusion: hematological factors can give a valuable for the detection of yeast infections.

Keywords: Yeast: COVID-19

The Association Between Dietary Inflammatory Index and Androgenic Alopecia in Fasa Adult Cohort Study: A cross-Sectional Study (Research Paper)

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Introduction: Androgenic alopecia (AGA) is the most common type of alopecia in both genders, affecting 80% of men and 40% of women till the age of 70 years. Increasing dihydrotestosterone (DHT), genetics, and unhealthy lifestyle. Inflammation plays a role in AGA pathogenesis. Bacterial colonization in the infundibulum may trigger inflammation by producing toxins and antigens. Also, keratinocytes may produce Interleukin-1a (IL-1a), reactive oxygen species (ROS), and nitric oxide in response to chemical stress from irritants, pollutants, and ultraviolet irradiation. IL-1a per se inhibits the hair growth cycle. Besides, this cytokine increases the inflammatory status in adjacent keratinocytes and makes them release other pro-inflammatory cytokines such as IL-1β and tumor necrosis factor α (TNFα). Finally, this low-grade chronic inflammation leads to perifollicular fibrosis. Previous studies showed that zinc, iron, and selenium are associated with AGA. Also, diets with low cholesterol and glycemic index have beneficial effects on AGA. Additionally, diet affects systemic inflammation. The dietary inflammatory index (DII) was developed to assess the inflammatory potential of diet. Higher scores of the DII indicate a pro-inflammatory diet and vice versa. Therefore, the present study aimed to investigate the association between DII and AGA.

Methods: This Cross-sectional study involved 10,318 from the Fasa Adult Cohort Study (FACS). After excluding the individuals with missing data or pregnancy, the remaining participants were divided into two groups based on

having androgenic alopecia (AGA), confirmed by an expert clinician. The DII was calculated based on the food frequency questionnaire with the global standard model developed by Shivappa et al. Then, the participants were divided into quartiles based on their DII scores. Age, gender, body mass index, smoking, opium, alcohol, educational status, occupational status, physical activity, marital status, and underlying diseases were considered as potential covariates. The potential covariates that had considerable differences (p-value < 0.2) between the two studied groups of AGA and non-AGA were included in the Wald Logistic Regression (WLR). Then, the covariates that were achieved as the most important covariates were adjusted in the final models. The crude and adjusted association of the DII Quartile with AGA were investigated using the Enter model of Logistic Regression. The significant level was considered as a P value < 0.05.

Results: The mean age of the final studied population (n=10,030) was 48.6 ± 9.6 years, including 4,523 men (45.1%). The mean DII was -0.27 ± 2.07, ranging from -6.50 to 5.66. Interestingly, 7,629 of the studied population (76.1%) had AGA. Also, 19.2% and 20.9% of the studied population was smoker and opium users. Participants in the 4th Quartile of the DII (pro-inflammatory diet) had a higher chance of having AGA (Odds Ratio: 1.294, 95% confidence interval: [1.13, 1.48], P value: <0.001) compared with 1st Quartile of the DII (anti-inflammatory diet). Among male participants, the adjusted model for age, education, smoking, opium consumption, socioeconomic status, and metabolic syndrome showed that the association of DII with AGA got stronger (Odds Ratio: 1.41, 95% Confidence Interval: [1.14, 1.75], P value: 0.002). However, in the case of women, adjusting for the same covariates made the association of DII with AGA insignificant (Odds Ratio: 0.95; 95% Confidence interval: [0.78, 1.16]; P value: 0.615).

Conclusion: A pro-inflammatory diet is associated with a higher risk of AGA in men, but not women. Therefore, an anti-inflammatory diet is beneficial for AGA prevention in men. Further studies are recommended to assess the association between the pro-inflammatory diet and AGA in women. Also, our findings added to the previous evidence about the influence of inflammation on the AGA.

Keywords: diet, inflammation, androgenic alopecia, pro-inflammatory diet

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The Association Between Energy-adjusted Dietary Inflammatory Index and Metabolic Syndrome: Fasa Adult Cohort Study (FACS) (Research Paper)

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Introduction: Metabolic Syndrome (MetS) serves as a combination of risk factors including low high-density lipoprotein-cholesterol and high fasting blood sugar, blood pressure, triglyceride, and waist circumference, that increase the probability of diabetes and cardiovascular disease. The prevalence of MetS has been reported between 20% and 45% and seems to have an incremental trend, reaching 53% in 2035. Improving lifestyle including a healthy diet and regular physical activity showed promising results for controlling MetS. Previous dietary interventions focused on decreasing energy intake, blood glucose, and triglyceride. Recent studies suggested that the anti-inflammatory nature of the Mediterranean diet has an effective role in MetS management. Also, inflammation plays an important role in the development and progression of obesity-related MetS and MetS complications such as cardiovascular diseases. The dietary inflammatory index (DII) was innovated to estimate the inflammatory potential of diet. As energy intake affects the inflammatory potential of diet, an energy-adjusted dietary inflammatory index (E-DII) was developed. Previous studies linked a pro-inflammatory diet with a higher risk of chronic diseases like diabetes, cancers, and cardiovascular diseases. Also, several studies investigated the association between DII and MetS. However, studies about the association of E-DII and MetS are scarce. The present study aimed to investigate the association between E-DII and MetS in the Fasa Adult Cohort Study (FACS).

Methods: This cross-sectional study was conducted on the FACS with 10,138 participants from Sheshdeh, Fasa, Iran. After excluding the participants with missing data, the remaining participants were divided into MetS and non-MetS. The sociodemographic characteristics, including, age (year), gender (men, women), ethnicity (Turkish, Arab, Fars, and others), marital status (single, married, widow, and divorced), occupation (having job or not), education (no education, primary school, secondary school, university), and physical activity (metabolic equivalent of tasks) was included. Also, the health status of participants including having cardiovascular disease, myocardial infarction, diabetes, hypertension, stroke, and fatty liver diseases were detected based on self-report, specialist diagnosis, medication, or recorded documents of participants. Anthropometric characteristics of each participant, including body mass index (kg/m2), waist, wrist, and hip circumference (cm), and systolic and diastolic blood pressure (mmHg) were measured and reported based on International Units. Fasting blood sugar (mg/dL), triglyceride (mmHg), and high-density lipoprotein-cholesterol (mmHg) were assessed using a plasma sample gathered at phase one and stored in the data bank of FACS. E-DII was calculated based on the recorded food frequency questionnaire. The MetS was assessed based on Adult Treatment Panel III criteria. The MetS is defined as having three or more out of these 5 items: 1) High waist circumference (>102 cm for men, > 88 cm for women); 2. High triglyceride (> 150 mg/dL); 3. low HDL-C (<40mg/dL for men and <50mg/dL for women); 4. High blood pressure (systolic >130mmHg or diastolic >85mmHg); 5. High fasting blood sugar (>100mg/dL). The data of the present study were recorded and analyzed in SPSS v.23. The qualitative and quantitative variables were reported as frequency (percent) and mean (standard deviation or standard error) or median (Quartile). Independent T-test and chi-square were used to compare the mean of quantitative and frequency of qualitative variables among MetS and non-MetS groups. The crude and adjusted association of EDII with MetS was investigated by logistic Regression (significant level: p-value<0.05).

Results: After exclusion, 10030 individuals (mean age of 48.6±10.0 years) including 4523 (45.1%) men were analyzed. The mean of EDII was -0.278±2.07, ranging from -6.5 to 5.6. Approximately 24% of participants had MetS. Individuals with MetS were more likely to be women, less educated, less physically active, and poor socioeconomically. However, smoking, opium, and alcohol consumption were significantly lower among individuals with MetS. They had a significantly higher rate of hypertension, myocardial infarction, diabetes, stroke, and fatty liver disease. The EDII was significantly associated with MetS (OR=1.55, 95%CI: [1.51, 1.59], p-value <0.001) and its components. Also, the result was consistent after adjusting for age, gender, education, physical activity, socioeconomic status, and smoking (OR=1.55,

95%CI: [1.51, 1.59], p-value < 0.001). The highest association was observed between EDII and high WC (OR =2.17, 95%CI: [2.08, 2.25], p-value = 0.000), as an indicator of obesity in MetS.

Conclusion: The pro-inflammatory diet is significantly associated with a higher risk of MetS. Therefore, an anti-inflammatory diet could prevent MetS and subsequently, its complications such as diabetes and cardiovascular diseases.

Keywords: health, nutrition, inflammation, metabolic syndrome

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The association between ox-LDL and cancer: an emerging targeted therapeutic approach (Review)

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Introduction: Lipids play an important role in varying vital cellular processes including cell growth and division. Elevated levels of LDL and oxidized-LDL and overexpression of the corresponding receptors including LDL receptor (LDLR), lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) and the cluster of differentiation 36 (CD36), showed a strong correlation with different facets of carcinogenesis including proliferation, invasion and angiogenesis. Further, the high serum level of LOX-1 is considered as a poor prognostic factor in many types of cancers including colorectal cancer.

Methods: Among the research papers published on PubMed, Web of Science, and Scopus databases between 2000 and 2023, the most relevant ones concerning the correlation between "ox-LDL," "cancer," and other pertinent phrases have been chosen.

Results: Ox-LDL could contribute to cancer progression and metastasis through endothelial-to-mesenchymal transition (EMT) and autophagy. Thus, many studies shed light on the significant role of ox-LDL as a suitable therapeutic target for cancer therapy. In Various repurposing approaches anti-dyslipidemia agents, phytochemicals, autophagy modulators as well as recently developed LDL nanoparticles have been investigated as potential tumor therapeutic agents by targeting oxidized-LDL/LOX-1 pathways. Herein, we have provided a concise summarization of the role of oxidized-LDL and LOX-1 in cancer progression, invasion, metastasis formation, and also cancer-associated angiogenesis. Further, we have addressed the therapeutic utility of several compounds that proved to be capable of targeting the metabolic moieties in cancer.

Conclusion: This review provides insights into the potential impact of targeting LDL and ox-LDL in cancer therapy and their future biomedical implementations.

Keywords: Ox-LDL; Carcinogenesis; Autophagy, LOX-1, LDL nanoparticles

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The association between serum calcium and phosphorus levels with gallstone disease in women: A case-control study (Research Paper)

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Introduction: Gallstone disease (GD) is a common health problem associated with the gastrointestinal tract. Some studies have investigated calcium and serum phosphorus levels in GD patients but the results are inconsistent. Therefore, this study was performed to define the association between serum calcium and phosphorus levels with GD risk among Iranian female patients.

Methods: This case-control study was performed among women including 75 patients with GD and 75 healthy controls in the Research Institute for Gastroenterology and Liver Diseases of Shahid Beheshti University of Medical Science in Tehran, Iran from October 2020 to March 2021. To measure serum calcium and phosphorus levels, blood samples were collected from all participants after 12 hours of fasting. To find the relationship between serum calcium and phosphorus levels and gallstone disease, multivariate logistic regression was used. This study was approved by the Ethical Committee of the Faculty of Nutrition and Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran (research ethics number: IR.TBZMED.REC.1398.1202).

Results: The results of the analysis showed an inverse significant association between serum phosphorus level (OR: 0.16; 95% CI: 0.03–0.78, p = 0.024) with GD; as well serum calcium (p = 0.023) and phosphorus (p = 0.020) levels were significantly higher in healthy subjects. No significant association was observed between serum calcium level and GD.

Conclusion: Present results suggested that higher serum phosphorus level was inversely associated with the risk of GD. To support these findings more studies are required.

Keywords: Gallstone disease, Serum calcium, serum phosphorus

The basis of Triple A syndrome; a large deletion in the AAAS gene causes the disease in a child (Research Paper)

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3.

Introduction: Triple A syndrome, also known as Allgrove syndrome, is a rare autosomal recessive disorder. It is characterized by a triad of symptoms: adrenal insufficiency (Addison's disease), alacrima (reduced or absent tear production), and achalasia (failure of the smooth muscles of the esophagus to relax). The condition tends to manifest in childhood or adolescence, and additional symptoms such as autonomic dysfunction and neurological abnormalities may also be present. This syndrome is an extremely rare condition, and its exact frequency is not well-established. Due to its rarity, it can often go undiagnosed or misdiagnosed, leading to challenges in gathering accurate data on its prevalence. Here, we have found an extensive large deletion in AAAS gene in a 5-year-old girl with adrenal insufficiency.

Methods: 1. Gene Selection for Assessment: Considering the clinical manifestations of the proband closely resembling triple A syndrome, we opted to investigate the importance of the AAAS gene on 12q13.13. This gene is widely recognized as the key determinant of Triple A syndrome. 2. Whole Exome Sequencing (WES): 2.1. Proband Sample: We collected peripheral blood from the proband and employed Whole Exome Sequencing using the Illumina HiSeq4000 platform. The sequencing process utilized a read length of 101 base pairs and achieved a coverage of 100x. The Laboratory for Molecular Diagnosis at the University of Leuven conducted this test. 2.2. Parental Samples: Since the couple previously had a male child with ambiguous genitalia, we requested Whole Exome Sequencing to analyze 219 genes associated with disorders of sex development. The objective was to identify potential single point mutations and small indels linked to this phenotype. For this purpose, we utilized the Twist Human Core Exome kit and performed library sequencing on the Illumina platform. The sequencing achieved a basic coverage of 316x with a mean no-target range of 102x. CeGaT GmbH in Germany conducted the sequencing. The NGS method's analytical sensitivity and specificity in the assay were assumed to be >95%. 3. Genomic Amplification by Polymerase Chain Reaction (GAP PCR) To

ascertain if the observed large deletion in the proband was a newly occurring mutation or one inherited from the parents, simultaneous Gap PCR was performed in the proband and the parents.

Results: A significant finding in this study was the identification of a homozygous large deletion spanning exons 3, 4, 5, 6, and 7 (MN_015665) of the AAAS gene. The deletion, located in the genomic region 12:53707985-53709653, is approximately 7000 bp in length. This deletion strongly correlates with the clinical manifestations observed, confirming a definitive diagnosis of Triple A syndrome in the proband. Interestingly, no mutations were detected in the sex development genes of the parents. The WES results did not reveal any large duplications, deletions, translocations, ploidy changes, or uniparental disomies associated with sex development disorders. However, two heterozygous variants of uncertain significance (VUS) were identified in the FRAS1 gene (c.2138-6C>T) and the TRIM32 gene (c.370C>T) specifically in the father's parents. Furthermore, the proband has inherited Triple A syndrome from her carrier parents, as confirmed by GAP PCR analysis. This analysis revealed a large heterogeneous deletion of the AAAS gene (region 12:53707985-53709653) in a homozygous form, matching the deletion identified in the proband's parents.

Conclusion: Our proband showed all three main clinical features and some other rare manifestations like hyperpigmentation. By identifying heterozygote disease-related mutations in the parents, prenatal diagnosis for later pregnancies was suggested for the couple.

Keywords: Triple A syndrome , ALADIN, AAAS gene, Alacrimia, Achalasia, Adrenal insufficiency

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The Cell Models of Cancer (Review)

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Introduction: Cell models of cancer have played a pivotal role in advancing our understanding of the complex processes underlying oncogenesis. This abstract provides a comprehensive overview of the diverse cell models used in cancer research, highlighting their importance in elucidating the molecular mechanisms of cancer initiation, progression, and treatment response.

Methods: This review extensively searched multiple databases such as Science Direct, Google Scholar, Pub-Med, and Web of Science, along with conducting a wide-ranging exploration of cell models. These cell models, including established cancer cell lines, patient-derived xenografts (PDX), three-dimensional organoids, and patient-derived organotypic cultures, have been employed to mimic the heterogeneity and complexity of human tumors. This abstract discusses the strengths and limitations of each model, emphasizing their utility in addressing specific research questions.

Results: Cell models of cancer have yielded crucial insights into the genetic and epigenetic alterations driving tumorigenesis, tumor heterogeneity, and drug response. They have been instrumental in identifying novel therapeutic targets and evaluating the efficacy of anticancer drugs. Moreover, advances in genome editing technologies, such as CRISPR-Cas9, have enabled the development of more precise and sophisticated cell models.

Conclusion: The use of cell models of cancer has significantly contributed to our understanding of the disease, facilitating the development of targeted therapies and personalized treatment approaches. However, it is essential to acknowledge the limitations and challenges associated with these models, including issues related to recapitulating the tumor microenvironment. Future research should continue to refine and innovate cell models to better mimic the complexity of human tumors, ultimately improving our ability to combat cancer.

Keywords: Oncogenesis, Tumor heterogeneity, Patient-derived xenografts, Tumor microenvironment

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The Clinical Utility of Virtual Reality in the clinical laboratory: A Systematic Review (Review)

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2. HIM Researcher

Introduction: This systematic review explores the benefits, limitations, and practical applications of VR in clinical laboratory settings through analysis of recent scientific literature.

Methods: Literature searches were conducted in 2019-2023 using PRISMA guidelines and keywords "clinical laboratory", "virtual reality", and "clinical utility". Studies published in the past 5 years were included to focus on recent research.

Results: Current findings highlight VR advantages in laboratory training and education, realistic skill simulations, diagnostic testing improvements, and laboratory automation advancements. However, limitations exist including lack of protocols, technological constraints, costs, and ethical considerations.

Conclusion: While more research is needed, VR demonstrates valuable potential to enhance laboratory practices through improved training, accuracy, efficiency, and workflow optimization. Careful development and evaluation is critical to address existing barriers to adoption.

Keywords: virtual reality, clinical laboratory, medical laboratory, clinical utility

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The Comparison of 940nm and 810nm Diode Laser Effects on the Repair of Inferior Alveolar Sensory Nerve Injury: A Clinical Trial (Research Paper)

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2.
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Introduction: The repair of the inferior alveolar sensory nerve is a major concern for dentists during dental procedures. Despite ongoing debates on various treatment modalities, this study aims to compare the effectiveness of 940nm and 810nm diode lasers on the repair of the nerve.

Methods: In this single-blinded randomized clinical trial, 39 patients with inferior alveolar nerve injury were divided into three groups: 1. 810nm laser irradiated, 2. 940nm laser irradiated, and 3. No laser irradiation (control group). All patients were treated in 12 sessions (3 days per week) and evaluated using a complete clinical neurosensory test (CNT), including brushstroke, 2-point discrimination, pinprick nociception, and thermal discrimination before and after treatment.

Results: The mean dysesthesia of the patient treated with 810nm diode laser was significantly lower than the control group in all sessions (the 1st ($p= 0.003$), 3rd ($p= 0.008$), 7th ($p= 0.006$), and 12th sessions ($p= 0.005$)). The 810nm laser resulted in more satisfaction in patients than the control group in almost all sessions (1st ($p< 0.001$), 7th ($p= 0.028$), and 12th ($p= 0.006$)). More patient satisfaction was seen in the 1st and 3rd sessions in the 810nm laser than in the 980nm laser ($p< 0.001$ and $p= 0.003$, respectively).

Conclusion: It has been observed that the 810nm diode laser may be more effective in repairing damage to the inferior alveolar sensory nerve compared to the 940nm diode laser.

Keywords: Semiconductor Diode Laser, GaAlAs lasers, Mandibular nerve injuries, Inferior alveolar nerve injury

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The correlation between Sex chromosomal abnormality and IVF technique (Research Paper)

Saghar Zonnar,[1] Parisa Esmaeili Kordlar,[2] Fatemeh Faghihi,[3,*]

1.
2.
3.

Introduction: The correlation between Sex chromosomal abnormality and IVF technique Saghar Zonnar1, Parisa Esmaeili Kordlar, Fatemeh Faghihi In vitro fertilization is the most commonly utilized assisted reproductive technology. ActuallyIn vitro fertilization (IVF), or in other words, the process of combining reproductive cells in a laboratory environment, applies to people who cannot have children naturally.However, the procedures can be intensive and costly, and success depends on various factors like age and number of cycles. An IVF treatment cycle can be separated into five steps: I. Ovarian stimulation and qualification which uses medications to increase the number of eggs available. II. Egg collection III.Fusion of ovum and sperm to create embryos in the laboratory, and freezing any suitable spare embryos. IV. Embryo transfer of one or sometimes two embryos into the uterus. V. Luteal phase, which covers preparing and maintaining the uterus to allow an embryo to implant and give rise to pregnancy. While IVF itself can cause a number of common chromosomal abnormalities, as well as sex chromosome syndromes. A 2019 national report published by SART (Society for Assisted Reproductive Technology) revealed age as a critical factor.For instance, According to the report, 55% of women under 35 achieved a live birth following one egg retrieval cycle. The percentage dropped to 4.3% for women over 42 year. Even though in NIPT test results,there is a significant relation between IVF,invalid gender and High risk in sex chromosome results. So, the correlation between of sex chromosomeabnormalitiesand IVF can be an important point to investigate. Key words: IVF technique, Sex Chromosome Abnormality, NIPT test 1. Sagharzonar1372@gmail.com

Methods: ELAISA technique, NGS technique, PCR

Results: The percentage dropped to 4.3% for women over 42 year. Even though in NIPT test results,there is a significant relation between IVF,invalid gender and High risk in sex chromosome results

Conclusion: So, the correlation between of sex chromosome abnormalities and IVF can be an important point to investigate.

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Keywords: IVF technique, Sex Chromosome Abnormality, NIPT test

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The Correlation of Septin4 Gene Expression with Sperm Quality, DNA Damage, and Oxidative Stress Level in infertile Patients (Research Paper)

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Introduction: Septin4 belong to a family of polymerizing GTP-binding proteins that are required for many cellular functions, such as membrane compartmentalization, vesicular trafficking, mitosis, and cytoskeletal remodeling. One family member, Septin4 (full name: Septin; symbol name: SEPT), is expressed specifically in the testis. The aim of the present study was to determine the association between Septin4 gene expression, sperm quality, DNA damage, and stress oxidative level in infertile patients.

Methods: The present study included 60 semen samples that were obtained from men attending the Infertility Research Center at the Academic Center for Education, Culture, and Research (ACECR) in Qom, Iran and were divided into three groups: Normozoospermia (n=20), Asthenozoospermia (n=20), Astheno-Teratozoospermia (n=20). Semen samples were collected and initial analysis including semen parameters was analyzed by using the World Health Organization protocol. The mRNA expression of Septin4 in sperm was examined using reverse transcription–polymerase chain reaction (RT-PCR). Oxidative stress markers, i.e. total antioxidant capacity (TAC), Superoxide dismutase(SOD), catalyzes(CAT), Glutathione peroxidase (GPX) and malondialdehyde (MDA), were determined by ELISA kit.

Results: The current study showed a statistically significant highly positive correlation in Septin4 gene expression with sperm motility, normal morphology, viability, capacity, and sperm Mitochondrial membrane potential. However, it shows significant negative correlation with sperm DNA fragmentation. Septin4 had a significant correlation with stress oxidative factor and antioxidant enzyme levels.

Conclusion: In conclusion, SEPTIN-4 gene expression provides clinical useful information for the diagnosis of male infertility. It might be a marker for discrimination between fertile and infertile patients.

Keywords: Septin4, Sperm quality, DNA damage, Stress oxidative

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The deadly trio, Edward's syndrome (Review)

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Introduction: Aneuploidy or the abnormal number of chromosomes can cause various disorders such as: spontaneous abortions, developmental defects and cancer. One of the types of aneuploidy is Edward's syndrome, which is discussed in this article. There are two important points about this syndrome. First, this syndrome is the second most common trisomy in the world after trisomy 21 or Down syndrome, and secondly, the exact mechanism of the cause of this syndrome has not yet been discovered. In this field, many articles have been written, especially in the form of examining different patients, but however, this issue has not been examined as it should be. In this article, we try to collect the information written in previous studies and prepare the ground for further research.

Methods: In order to write this article, we first studied general and basic information on the Internet and then reviewed and studied articles in Google Scholar from 2019 until now. In the search of articles, we also used terms such as: Edward's syndrome, Edward's syndrome genetics, Edward's syndrome symptoms and Edward's syndrome treatment and the prevalence of trisomy 18.

Results: Edward's syndrome was first defined in the 1960s. This syndrome is known as the second most common trisomy, and the prevalence of this syndrome among newborns is 1/1600 to 1/1800, but due to many abortions, as well as its diagnosis and termination of pregnancy, the number of these babies has reached 1/3600. and the prevalence of Edward's syndrome in girls is 3 times that of boys. Edward's syndrome is one of the prominent aneuploidies in the world. In this syndrome, there are 3 of chromosome 18 and it is actually a type of trisomy. In general, trisomies cause disturbances in the cell cycle, such as reducing the ability of somatic cells to reproduce. The cause of this syndrome is either the lack of correct segregation of chromosomes during meiosis, especially from the maternal side (94%) or less commonly post zygotic nondisjunction mitosis. However, the exact mechanism of trisomy 18 is not known. Genetically, trisomy 18 can be in the following three forms: 1) a complete extra chromosome 2) a partial trisomy (18q) 3) or a mosaic This trisomy causes a significant increase in mortality in

sufferers, so that only 5 to 10% of sufferers survive after one year of age, but on the other hand, even though this syndrome is associated with a high risk of stillbirth and fetal loss, more than 50% of patients survive for more than a week. In the past, this disease was called "incompatible with life" and special treatment methods were not prescribed for the sufferers, but temporary sedatives were prescribed by the medical community, but today, researchers of treatment methods to correct congenital anomalies (medical and surgical interventions) especially Cardiac abnormalities have been presented to increase the survival of this baby. It is noteworthy that the prevalence of this trisomy increases with the age of the mother. The symptoms of this syndrome include: incomplete heart, digestive defects, abnormalities of the stomach, esophagus and endocrine glands, hearing and vision disorders, kidney disorders, abnormalities of the nervous system, mental retardation, drooping ears and bent fingers.

Conclusion: Congenital abnormalities such as the topic discussed in this article impose heavy economic, social and cultural consequences on the family and society, therefore, early diagnosis and termination of pregnancy is very important. Therefore, in this article, we did a general review of this trisomy and its symptoms. It is expected that in the future researches, methods of prevention and early diagnosis of this disorder will be worked on. Also, an important defect in this field is the reason for the occurrence of this syndrome and its exact mechanism, and also methods for treating or increasing the life span of the sufferers can be found. important and vital issues for the continuation of the research process.

Keywords: Edward's syndrome / trisomy 18 / non-disjunction

The demographic risk factors of pro-inflammatory diet: A Cross-sectional Study on Fasa Adults Cohort Study (FACS) (Research Paper)

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Introduction: Considering the effect of micro- and macro-nutrients such as carbohydrates, fiber, fatty acids, vitamin B12, niacin, zinc, etc., and energy intake on inflammatory biomarkers, the Dietary Inflammatory Index (DII) was developed to indicate diet's pro- or anti-inflammatory effects. The association between the pro-inflammatory diet and chronic diseases has been an attractive topic for researchers in the last few years. Several studies have linked the pro-inflammatory diet (higher DII) with chronic diseases, such as diabetes, cardiovascular diseases, and cancers. However, there is limited evidence addressing the sociodemographic risk factors for a pro-inflammatory diet. To prevent chronic diseases through dietary interventions, it is necessary to determine the high-risk populations for consuming a pro-inflammatory diet who are vulnerable to chronic noncommunicable diseases, but the findings about the risk factors of the pro-inflammatory diet are still limited to the crude associations investigated in some studies.

Methods: This cross-sectional study was conducted on the FACS with 10,138 participants from Sheshdeh, Fasa, Iran. After excluding the participants with missing data, the remaining participants were divided into a pro-inflammatory diet (higher than the median of DII) and an anti-inflammatory diet (higher than the median of DII). The sociodemographic characteristics, including, age

(year), gender (men, women), ethnicity (Turkish, Arab, Fars, and others), marital status (single, married, widow, and divorced), occupation (having job or not), education (no education, primary school, secondary school, university), and physical activity (metabolic equivalent of tasks) was included. Also, the Dietary Inflammatory Index was calculated based on the Shivappa et al. study in 2013. The data of the present study were recorded and analyzed in SPSS v.23. The qualitative and quantitative variables were reported as frequency (percent) and mean (standard deviation or standard error) or median (Quartile). The Wald regression model was used to investigate the most associated features among included demographic variables. The significant level was considered as a P value < 0.05.

Results: The final studied population (10030 participants with a mean age of 48.6±10.0 years) included 4523 (45.1%) men. The mean of EDII was -0.278±2.07, ranging from -6.5 to 5.6. The Wald Regression revealed that being a man (OR: 1.120, 95%Confidence Interval: [1.005,1.248], P-value: 0.040) and having higher age (OR: 1.011, 95%Confidence Interval: [1006, 1.015], P-value: <0.001), lower physical activity (OR: 0.988, 95%Confidence Interval: [0.984, 0.992], P-value:<0.001), better socioeconomic status (OR: 1.094, 95%Confidence Interval: [1.072,1.115], P-value:<0.001), and having no job (OR: 1.183, 95%Confidence Interval: [1.055,1.327], P-value:0.004) had the most significant association with pro-inflammatory diet.

Conclusion: The present study showed that demographic features had an important role in having a pro-inflammatory diet. Therefore, further studies are required to focus on the mechanism of these differences and design further nutritional interventions to provide an anti-inflammatory for these vulnerable groups.

Keywords: nutrition, prevention, public health, demographic features

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The development of a thermosensitive and bioadhesive nanotransfersome–hydrogel hybrid system for enhanced skin bioavailability and antibacterial activity of cephalexin (Research Paper)

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Introduction: Cellulitis is a common bacterial infection of the skin and soft tissues immediately beneath the skin. Despite the successful use of antibiotics in the treatment of infectious diseases, bacterial infections continue to impose significant global health challenges because of the rapid emergence of antibiotic resistance.

Methods: The aim of this work was to develop an in situ hydrogel forming system containing highly permeable cephalexin-loaded nanotransfersomes (NTs), suitable for antibacterial drug delivery. Response surface design was applied for the optimization of NTs. Cephalexin NTs were prepared using the thin-film hydration method and then embedded into a 3D hydrogel network. The in vitro antibacterial activity of the optimized NTs was assayed against indicator bacteria of Staphylococcus aureus (S. aureus). Drug permeability was evaluated using an ex vivo rat skin model. The in vivo efficacy of the cephalexin NT hydrogel was also determined against rat skin infection.

Results: The resulting data verified the formation of NTs, the size of which was approximately 192 nm. The cephalexin NTs exhibited higher antibacterial activity against S. aureus as compared to the untreated drug. The NT hydrogel improved drug penetration through the skin after 8 h. When applied on the rat skin for 10 days, the cephalexin NT hydrogel exhibited superior antibacterial activity with normal hair growth and skin appearance as compared with the plain drug hydrogel.

Conclusion: These findings suggest that the cephalexin NT–hydrogel system can serve as a valuable drug delivery platform against bacterial infections.

Keywords: Cellulitis; Cephalexin; Hydrogel; Nanotransfersome; Skin infection

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The effect of nanomedicine on glioblastoma treatment (Review)

Hoda Jomepour,[1,*]

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Introduction: Gboxin suppresses the growth of glioblastoma (GBM) cells by inhibiting a stage of respiration (oxidative phosphorylation) that occurs in mitochondria . And its anti-GBM effect is seriously limited by poor blood circulation, the blood brain barrier (BBB) and non-specific GBM tissue uptake, leading to insufficient Gboxin accumulation at GBM sites. we have found there is a delivery system that helps transport Gboxin to the target mitochondria using a membrane containing both cancer cell and mitochondrial membrane features. Using this delivery method. We present a biomimetic nanomedicine (HM-NPs@G) by coating cancer cell-mitochondria hybrid membrane (HM) on the surface of Gboxin-loaded nanoparticles. The HM camouflaging endows HM-NPs@G with unique features including good biocompatibility, improved pharmacokinetic profile, efficient BBB permeability and homotypic dual tumour cell and mitochondria targeting. Finally we achieved potent GBM tumour inhibition in vitro and in vivo leading to prolonged median survival time in mouse models.

Methods: Here we present a cancer cell-mitochondria hybrid membrane camouflaged reactive oxygen species (ROS)-responsive nanoparticle loaded with Gboxin (HM-NPs@G) to achieve targeting delivery of Gboxin in GBM mitochondria in non-invasive manner. The HM-NPs@G retain characteristic capabilities derived from each individual membrane type. The outer shell of the HM-NPs@G include multiple “self-marker” proteins embedded in both membranes which should improve the short blood circulation of Gboxin, leading to evasion of immune system clearance. And thre is a fact that mitochondria generate approximately 90% of intracellular ROS and that cancer cells have higher ROS levels than metabolically ‘quieter’ normal cells to leverage fast, at-site and Gboxin release using a ROS-responsive polymer. The accelerated release of Gboxin interrupts the functioning of ATP synthase at the mitochondria inner membrane, which results in disrupted electron transport and energy metabolism ultimately leading to mitochondria-mediated apoptosis in tumour cells.

Results: The fabrication of HM-NPs@G consists of two steps. First, the outer shell of cancer cell-mitochondria hybrid membrane (HM) was prepared using a one:one protein weight ratio of MM (mitochondria membrane) to CM (cancer membrane) as optimized and further characterized by förster resonance

energy transfer (FRET). he core-shell structure of the developed HM-NPs@G was confirmed with the transmission electron microscopy (TEM) and also indicating the hybrid membrane is a single-membrane lipid bilayer which is agree with the reported results.The proteins (EpCAM and Integrin αv) which play vital roles in cancer homologous targeting were observed on U87MG cancer cell membrane (CM). Furthermore, glioblastoma stem cell (GSCs, X01) membrane CM (X01) had CD44, one of stem markers, as well as EpCAM, both of which were helpful to target homotypic cells.

Conclusion: We have found that the use of the novel therapeutic VT1021 in patients with recurrent glioblastoma (rGBM) showed durable responses by inhibiting the tumour growth via stimulation of thrombospondin-1, which altered the tumour microenvironment. And also long-term findings showed that patients with a better immune response throughout treatment had better results compared with those who did not exhibit much of an immune response. Finally after the NPs were coated with membranes we indicate successful shielding of nanoparticles by the negative outer membranes.

Keywords: nano medicine- Gboxin - HM-NPs@G - glioblastoma- treatment

The effect of -196 C>T mutation on Aγ and Gγ-globin in k562 (Research Paper)

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Introduction: The -196 C>T mutation is a non-deletional hereditary persistence of fetal hemoglobin (ndHPFH) mutation that increases the amount of human fetal hemoglobin (HbF) by disturbing the Zinc Finger and BTB Domain Containing 7A (ZBTB7A) transcription factor binding site. Observations have shown that individuals with the -196 C>T mutation in their Aγ-globin promoter have greater fetal hemoglobin levels than persons with the mutation in their Gγ-globin promoter (Wienert, Martyn, Funnell, Quinlan, & Crossley, 2018). Given that the promoters of these genes are identical up until the -200 region, this discrepancy may be caused by the differential existence of the -196 C>T mutation in the Aγ or Gγ promoters. In order to investigate this disparity, we introduced the -196 C>T mutation into the left homology arm (i.e., Gγ or Aγ promoters) of a cassette containing EGFP and Neomycin resistance gene (NeoR). These modified EGFP cassettes were then knocked into the γ-globin gene(s) of K562 cells. Finally, EGFP fluorescence levels were assessed in the subsequent cell lines.

Methods: First, a previously assembled plasmid (Jafari, Hesami, Safi, Ghasemi, & Banan, 2019) includes an EGFP. (IRES). NeoR. pA cassette (IRES stands for internal ribosome entry site, and pA signifies a polyadenylation signal sequence), with flanking Left and Right homology arms (LHA and RHA) corresponding to the Gγ-globin gene was used to create the plasmid containing the Aγ-globin specific left homology arm, therefore, the Gγ specific LHA was removed through enzymatic digestion and then the Aγ specific LHA which was PCR amplified from K562 genomic DNA was cloned into the plasmid. Subsequently, these two plasmids harboring either Aγ or Gγ Left homology arms were used as templates in the overlap-PCR (Heckman & Pease, 2007; Vallejo, Pogulis, & Pease, 2008) to generate two distinct LHA

fragments containing the Aγ -196 C>T and Gγ -196C>T ndHPFH mutations, then these two LHA fragment were replaced the original LHAs in the EGFP plasmids, and by Sanger sequencing and restriction enzyme mapping the accuracy of products was verified. Following the Creation of mutated EGFP plasmids, these two plasmids alongside the CRISPR/Cas9 PX459 plasmid (RRID: Addgene_62988) (Jafari et al., 2019) harboring the gamma-globin-specific sgRNA were co-transfected into K562 cell by using Lipofectamine 2000. In parallel, the original EGFP plasmids without mutations were also co-transfected to produce control cell lines so that we could compare the effect of mutation with control cell lines. After selection through puromycin dihydrochloride (resistance in the CRISPR plasmid) and G418 (resistance in the EGFP plasmid), DNA was extracted from these cell lines to verify the target integration. Finally, Fluorescence levels were assessed in all these four cell lines.

Results: The Sanger sequencing readouts confirmed the target integration of -196 C>T and WT promoters into either the Aγ or the Gγ genes. The percentage of EGFP+ cells was 90% for Aγ-196 C>T HPFH mutation and 60% for WT: Aγ promoter. For Gγ-196 C>T HPFH mutation and WT: Gγ promoter, the percentages were 75% and 83% respectively. In terms of fluorescence intensity, the Gγ-196 C>T mutation caused no change compared to control cells, while the Aγ-196 C>T HPFH mutation decreased fluorescence levels compared to WT: Aγ control cells.

Conclusion: The -196 C>T mutation has been previously reported to disturb the binding site of the ZBTB7A transcription factor in adult erythroid cells and increase the amount of γ-globin gene production (Martyn et al., 2018; Mingoia et al., 2021; Weber et al., 2020), however, this was not the case in our study on fetal-like K562 cells, nevertheless, our results are consistence with research results of studies that are done on K562 cells. A study reports unchanged γ-globin expression after ZBTB7A knock-down which is in line with our result on Gγ (Chondrou et al., 2022). Another study indicated a reduction in γ-globin expression after ZBTB7A knock-out which is compatible with our result on Aγ-globin (Kang et al., 2019), therefore, it seems that the mutation has different consequences in adult and fetal cell line models, suggesting the possible different functions of the ZBTB7A factor during adult and fetal stages. Finally, our result indicates the difference between the effect of the -196 C>T Gγ and Aγ mutations, but it cannot explain the difference between individuals with the mutation in Gγ and Aγ, proposing further investigations on adult model cell lines.

Keywords: ndHPFH; CRISPR/Cas9; ZBTB7A

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The effect of anti-thyroid cancer drugs on laminin protein by molecular docking method (Research Paper)

Mahdiyeh Gholaminezhad estalkhjani,[1,*]

1. -

Introduction: Laminin is one of the main proteins of the basement membrane and According to research is a target for thyroid cancer treatment . Sorafenib is used in the therapy of advanced renal cell, liver and thyroid cancer . Doxorubicin is an antibiotic in the treatment of many cancers, including blood , breast, stomach , uterine , ovarian , lung and thyroid cancer. Vandetanib is a drug that is used to treat medullary thyroid cancer that cannot be treated with surgery or has spread to other parts of the body. Sunitinib is a medicine which is used in the treatment of gastrointestinal tract, kidney, pancreas and advanced thyroid cancer .

Methods: First, prepared the three-dimensional structure of the laminin protein by using the Uniprot site . Then, we obtain the three-dimensional structure of Sorafenib- Doxorubicin - sunitinib and Vandetanib drugs through the Pubchem site. In the next step, using the Chimera 1.10.2 program, we include changes such as removing ions, adding hydrogen, removing extra chains, etc. in the original protein . Finally, with the PyRx program, we start docking by loading the modified protein file as macromolecule and the drug file as input .

Results: protein = laminin (LAMC1) Drug Binding Affinity (kcal/mol) RMSD bound sorfenib 10- 0 Doxorubicin 9.2- 0 Vandetanib 7.8- 0 Sunitinib 7.6- 0

Conclusion: According to the investigations, sorfanib has the most effect on laminin protein, and Doxorubicin , Vandetanib and sunitinib have the most effect, respectively .

Keywords: unti-thyroid cancer drugs laminin protein molecular docking thyroid cancer

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The effect of astaxanthin on the proliferation of stem cells derived from mouse adipose tissue (Review)

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Introduction: Stem cells derived from adipose tissue of adult mice have the ability to differentiate into nerve and glial cells. The ability to differentiate these cells into all types of cells, especially nerve cells, has been proven in laboratory conditions. But the examination of cells after the transplantation of these cells in animal models of the diseasehas shown that only the MS A small percentage of cells transplanted to myelin-forming cells have developed as a result of using another supplement such as astaxanthin.(astaxanthin)which can improve the results of cell transplantation seems necessary.

Methods: In this review article, we have used the experiments and results of other scientists to better understand the article. Therefore, this article is a complete review. stem cells were isolated from the adipose tissue of the groin area and the back of the rat kidney After disassembly and inspectionmarkers, these cells for 72 hours in CD mediumand in the presence of a concentration of DMEM-F12 different types of astaxanthin)were cultivated Then at the end of reproduction and viability (10ng/ml), (5ng/ml), (1ng/ml) cells using the methodwas evaluated and evaluated by MTT.

Results: The results showed that a high percentage of cells(Mouse adipose derived stem cells, MADSCs markersAnd a low percentage of them expressed hematopoietic cell markers. In addition, the average survival percentage of CD 44 and CD90 in cells treated with5 ng of astaxanthin increased significantly compared to other groups (P=0.04)

Conclusion: Astaxanthin is able to increase the survival and proliferation of cellsand this substance can be used in the treatment of MADSCs Neurodegenerative diseases in diseaseUsed MS.

Keywords: Cell proliferation/astaxanthin/stem cells/multiple sclerosisMS (Multiple Sclerosis)

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The effect of Boswellia (Frankincense) on Multiple Sclerosis (MS) (Review)

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Introduction: Multiple sclerosis (MS) is a complex autoimmune disorder which characterized by demyelination and axonal loss in the central nervous system (CNS). Several evidences indicate that some new drugs and stem cell therapy have opened a new horizon for multiple sclerosis treatment, but current therapies are partially effective or not safe in the long term. Recently, herbal therapies represent a promising therapeutic approach for multiple sclerosis disease. Here we examine the effect of Boswellia (frankincense) plant on multiple sclerosis. Boswellia has been shown to have anti-inflammatory effects and neuroprotective activity and the Boswellia species, having neuroprotective potential, makes them a promising candidate to cure or prevent the neurodegenerative disorders.

Methods: In Google Scholar and PubMed databases, we searched the keywords "Boswellia and Multiple Sclerosis" and "Frankincense and Multiple Sclerosis" and collected articles related to these keywords and wrote this article by studying them.

Results: According to the research conducted by researchers on the effect of Boswellia (frankincense) on multiple sclerosis, acceptable results were obtained. One of the most important results obtained is the reversal of cognitive impairment in patients with multiple sclerosis, which is due to the anti-inflammatory and neuroprotective properties of Boswellia. Also, patients with MS who received Boswellia, had a significant visuospatial memory improvement compared to the control group.

Conclusion: According to the results obtained in the research, it can be concluded that the Boswellia (frankincense) plant is effective in the treatment of MS with its anti-inflammatory, neuroprotective and reversing cognitive impairment of people with MS and other properties.

Keywords: Boswellia, Multiple sclerosis, Frankincense

The effect of Cancer Stem Cells on Tumor Growth and Cancer (Review)

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Introduction: Cancer stem cells (CSCs) are a small subpopulation of self-renewing malignant and oncogenic cells that drive tumor initiation and progression. CSCs play pivotal roles in tumor initiation, progression, cell death resistance, therapy resistance, and tumor recurrence following treatment and remission. Tumor initiation can either be driven by transformed differentiated cells or transformed tissue resident stem cells. Recent research has identified and isolated cancer stem cells (CSCs), which are considered one of the primary causes of resistance to oncological treatments, and contribute to local and distant recurrence. Studies have shown that stem cells and progenitor cells in normal tissues are susceptible to carcinogenic transformation.

Methods: In the current study, keywords including Cancer Stem Cells, Tumor Growth, and Metastasis were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized. The searches comprised all published papers from 2000 to 2023. All of full text was considered and the papers manifested as only abstract was excluded. The full papers selected that specific effect on cancers only. Totally 50 papers were selected and studied in this review.

Results: Recent growing evidence suggest that the tumor is composed of heterogeneous populations of cells with different levels of malignity and the tumor development is driven by a specialized cell subset, characterized by self-renewing, multi-potent, and tumor initiating properties. In colon cancers, recent studies in mice have shown that even differentiated intestinal epithelial cells can be potential CSCs. In squamous cell carcinomas the differentiation phenotype seems to be influenced by the cell of origin and the kind of driver mutation, both responsible for the invasiveness and aggressiveness of the tumor. Tumors generated based on CSCs are believed to follow a unidirectional hierarchy, in which only the CSC population can initiate tumor growth. One article reported the dualistic origin of human tumors, suggesting that tumors could arise from blastomeres generated from fertilized eggs, and

stem cells generated from reprogrammed somatic cells. Also, CSCs have been identified in tumors of the liver, pancreas, breast, brain, lung, and ovary. Induction of lung cancer in animal models using genetic modification suggests that lung cancer originates from resident stem cells. Other research demonstrated Mesenchymal stem cells (MSCs) that produce VEGF, Angiopoietin-1 (Ang-1) and other pro-angiogenic factors, could differentiate into pericytes and endothelial cells, which support tumor vascularization and growth.

Conclusion: CSCs are capable of generating an entire tumor and tend to be more chemo- and radioresistant due to their quiescent state and upregulation of efflux pumps. CSCs also, can evade the immune system, have efficient DNA damage repair mechanisms, and can easily adapt to hostile environments. Consequently, CSCs have been implicated in tumor recurrence, chemoresistance, metastasis, and thus poor clinical outcomes.

Keywords: Cancer Stem Cells, Tumor Growth, and Metastasis

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The effect of curcumin nanomicelle on embryo quality in women with Endometersis: a randomized controlled trial (Research Paper)

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Introduction: Endometriosis is one of the main common gynecological disorders, which is characterized by the presence of glands and stroma outside the uterine cavity. Some findings have highlighted the main role of inflammation in endometriosis by acting on proliferation, apoptosis and angiogenesis. Oxidative stress, an imbalance between reactive oxygen species and antioxidants, could have a key role in the initiation and progression of endometriosis by resulting in inflammatory responses in the peritoneal cavity. In this study, The effect of curcumin nanomicelle on embryo quality in women with Endometersis.

Methods: This clinical trial was conducted on 10 women with Endometersis, diagnosed according to the Rotterdam criteria, who were sequentially recruited and randomly divided into two groups (n = 5 each). group 1 received 80 mg/day curcumin nanomicelle three times daily, and group 2 (control group) not received curcumin nanomicelle. Data were analyzed by one-way ANOVA, with significance set at $P < 0.05$.

Results: The number of immature and abnormal oocytes decreased significantly in the treatment compared with control group ($p<0.05$), but a concomitant increase in the fertilization rate, cleavage rate, and number of good-quality embryos in the treatment group ($P < 0.05$). Malondialdehyde

levels decreased significantly in the curcumin nanomicelle group compared with the control group ($P < 0.05$). In addition, there were significant decreases in leptin levels in the treatment group compared with the control group ($P < 0.05$). Insulin and LH levels were significantly lower in the curcumin nanomicelle group compared with the control group ($P < 0.05$).

Conclusion: We concluded that curcumin nanomicelle improves oocyte and embryo quality in women with Endometersis.

Keywords: Curcumin nanomicelle, Endometersis, Embryo quality

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The effect of DNA in reversing the aging process (Review)

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Introduction: Dealing with aging and reversing its process is always one of the conditions that mankind is looking for a solution for. In the last decade, in order to achieve this goal, research is done by examining DNA and its methylation. The study focused on physiological rejuvenation and analysis of specific and well-established epigenomic signatures of aging. The study suggests that chemical reprogramming may be used to treat blindness, liver failure, and skin damage. However, it is critical that the safety of chemical rejuvenation cocktails is tested rigorously in mammalian animal models before human trials are initiated.

Methods: For this research, various tests, including nuclear counterstaining with Hoechst 33342, wide field fluorescence imaging using the IXM-LZR, RNA sequencing and analysis using the Omega ENZA Total RNA kit, Agilent Tapestation, Illumina Novaseq, FastQC. Genetic material has been used in some approaches to reverse aging, such as adeno-associated viral (AAV) delivery of DNA and lipid nanoparticle-mediated delivery of RNA. However, the delivery of genetic material can face potential barriers, including high costs and safety concerns associated with introducing genetic material into the body.

Results: Developing a chemical alternative to mimic the rejuvenating effects of genetic material could potentially delay aging and enable the treatment of various medical conditions.

Conclusion: chemically induced reprogramming to reverse cellular aging involves the use of a cocktail of small molecules, That includes various chemicals such as VPA, CHIR99021, Repsox-616452, Tranylcypromine, Forskolin, Sodium Butyrate, bFGF, TTNPB, Y27632, SAG, ABT869, and α-KG. These chemicals work together to induce partial reprogramming of cells, which can reset the epigenome to a more youthful state and reverse cellular aging.

Keywords: DNA-RNA-Methylation-Material-Rejuvenation

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The effect of exposure to opioids during fetal period on the brain (Review)

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Introduction: Exposure to opioids in embryonic period is a global phenomenon. Given that pregnancy is a very important period in the life of mother and fetus and central nervous system is one of the first targets of injury in drug abuse, the importance of pregnancy is more obvious. The duration of the exposure, amount and type of substances that enter the blood and central nervous system of the fetus are among the variables that affect the effects of drugs. Just as the amount of absorption by mouth, inhalation, smoking, and injection are not the same, the effects on the vital organs of the fetus and its toxicity are different. Exposure to drugs before birth delays the development of the brain and neural structures during or after birth. The noradrenergic system plays a role in regulating neurological growth during development, which is essential for maintaining normal functioning of the central nervous system. It is also involved in many cognitive processes such as attention and working memory. Therefore, changing norepinephrine levels can lead to deficits in attention. Exposure to opioids in mid-pregnancy to late pregnancy induces long-term, gender-dependent neurochemical changes in the noradrenergic system of male and female adult rats. In male rats, prenatal exposure to opioids increases noradrenaline content and its production and secretion and tyrosine hydroxylase, a key enzyme of catechol amines biosynthesis. These indices decrease in female animals (Alaie et al., 2021).

Methods: The content of this article has been obtained from the study of various books and articles.

Results: Pro encephalin gene expression decreased in male rats exposed to opioids before birth in the pre-visual region and in female rats in the ventral medial nucleus of hypothalamus. Opioids increase dopamine release in several areas of the brain. During development, dopamine acts as a growth regulator and influences neural development. Since dopaminergic system is involved in cognitive processes such as attention, working memory, and inhibitory control, children who have been exposed to methadone before birth are susceptible to attention disorders, obsessive-compulsive behaviors, deficits in executive functions, and it seems that mesolimbic dopaminergic system plays an important role among several neurotransmitter motor skills involved in reward and reinforcement process.

Conclusion: Prenatal exposure to opioids causes a decrease regulation of dopamine receptor expression gene in adult offspring that affects neonatal cognitive development such as memory and learning, attention, language, problem-solving skills and executive activities by damaging the central nervous system of the fetus. Also, studies in rats show that oral administration of morphine by pregnant mother delays development of lateral ventricle and fetal choroid plexus appendix cells. On the other hand ،this effect may lead to abnormal function of these cells ،namely cerebrospinal fluid secretion and blood supply of brain cells. Any decrease or increase in cerebrospinal fluid by the ependyma cells of the choroid plexus causes abnormalities including hydrocephalus and enlargement of the cerebral ventricles. Considering the effect of maternal addiction on all aspects of children's health and susceptibility to addiction later in life, attention to prevention, treatment and control of substance abuse in pregnancy care is essential.

Keywords: Drugs, Fetal Age, Brain

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The Effect of Game-based Virtual Reality Applications on the Learning of Medical Sciences Students (Review)

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Introduction: Virtual Reality (VR) can be used as a digital educational tool for learning and assessment because it produces a virtual replica of the real world. It uses computer technology to create a 3D image or environment which allows the students to interact with in a way that appears to be real or physical. Game-based VR applications can help students get prepared for clinical applications and improve their knowledge of standard precautions. The aim of this review study is to investigate the effect of game-based virtual reality applications on the learning of medical sciences students.

Methods: This review study was conducted through an advanced search in reputable scientific databases including PubMed, Scopus, Eric, Web of Sciences, SID and Google Scholar search engine from 2018 to May 2023 using keywords “Virtual Reality”, “Education”, “Medical Students” and their Mesh terms. After the initial search, screening was done in two stages: first, primary screening was done (inclusion criteria such as English-language studies, original, intervention, and observation articles). Then the secondary screening was done (the title and abstract were relevant to the education of medical sciences students such as medical students, residents, nursing students, etc. and irrelevant articles were removed). The articles related to the study were also evaluated through a researcher made evaluating tool. Finally, articles were extracted initially and combined data from articles that met the inclusion criteria (14 articles).

Results: The results of this study suggest that a higher success rate is achieved for students training in VR than students trained in traditional methods. It was shown that the undergraduate students, postgraduate students and hospital residents using VR technology had a higher passed rate. Learning complex skills and specialized knowledge can be achieved through virtual reality training. Real-time feedback, combined with 3D

computer-generated scenery, enabled students to use VR technology to improve their autonomic knowledge. Using VR, students practiced surgery and made fewer mistakes than they could have in a real operating room. Students also express greater confidence in their abilities to complete the tasks they were trained to do and are more knowledgeable about the processes involved.

Conclusion: The game-based virtual reality applications were effective in teaching different skills for medical science students in the short term. In addition to facilitating learning, virtual reality technology can complement current educational approaches and provide medical sciences educators with novel and engaging ways to deliver content. It is recommended that such VR applications be used in psychomotor skill training.

Keywords: Virtual Reality, Learning, Medical Education, Medical Students

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The effect of green tea EGCG on the expression of growth factor receptors and PI3K pathway in the androgen-dependent LNCaP cells (Research Paper)

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Introduction: Different signaling pathways have been demonstrated to be involved in the pathogenesis of human cancers. Several studies indicated that the abnormal expression of growth factor receptors and PI3K signaling pathway genes plays an important role in the cell survival and proliferation of prostate cancer cells. In the present study, the effect of EGCG, a major component of green tea, was studied on the expression of PI3K, AKT, mTOR, EGFR, MET, IGF1R and FGFR1 in the prostate cancer LNCaP cells.

Methods: For this purpose, LNCaP cells were treated with different concentrations of EGCG. After 48 and 72 hours, the cell viability of treated cells was evaluated by MTT assay. Then, RNA was extracted from the LNCaP cells treated by EGCG concentrations which was associated with the significant reduction in cell viability (<0.05). After removing DNA contamination and synthesis of cDNA, the expression of PI3K, AKT, mTOR, EGFR, MET, IGF1R and FGFR1 was determined by Real time PCR.

Results: The analysis of data showed that treatment with 200μM EGCG for 72 hours significantly diminished the expression of AKT, EGFR and FGFR1 genes in the androgen-dependent LNCaP cells. Furthermore, the decreased expression of AKT and IGF1R was observed in the LNCaP cells treated with 500μM EGCG for 72 hours ($p<0.05$).

Conclusion: The obtained results suggested that EGCG reduced the survival of LNCaP cells through the downregulation of AKT, EGFR, FGFR1 and IGF1R genes

Keywords: EGCG, Prostate cancer, PI3K pathways, Growth factor receptors, LNCaP cells

The effect of insomnia on bipolar disease (Review)

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Introduction: Bipolar disorder (BD) is a relatively common chronic mood disorder characterized by cyclic periods of depression, mania/hypomania. The average age of onset of BD is approximately 20 years.The lifetime prevalence of BD in the population is estimated to be 1-2% worldwide. Bipolar disorder is the same in both sexes. BD has two distinct subtypes: subtypes 1 and 2.(1) (2) - The genetic talent for BD is considered high (73-93%). The difference between the subtypes is that type 1 is consistent with manic and depressive episodes, while type 2 includes hypomanic and depressive episodes. Manic periods are characterized by hyperstimulated mood), increased energy, decreased need for sleep, impulsive behaviors, fast and abundant speech, multiple purposeful ideas. In the manic period, psychotic symptoms may appear. Hypomania can be considered a milder version of mania, the daily activity of the patient is controllable and does not cause any psychotic symptoms. Depressive episodes include low mood, persistent sadness, lack of interest in activities that were previously experienced as interesting, sleep disturbances, feelings of worthlessness or even hatred, suicidal thoughts, and decreased will to live. Characterized. Depression periods usually last about 6 months, but due to the longer duration of depression, patients spend much more time in depression compared to mania.(3) In people with bipolar disorder, there is a normal and calm mental state or mood, which is neither mania nor depression, and it is called etmia.

Methods: Because the article is a review, it does not have methods

Results: Patients whose sleep changes from one week to another can be chronic in causing mood changes,The relationship between sleep and mood symptoms on both sides.(5) We found stronger associations between sleep and hypomania in individuals with BD1 and stronger associations of depression with insomnia in individuals with BD2. They also found strong relationships for education based on sex (strong relationships and sleep and hypomania for women) and age (strong relationships between sleep and injury in young people)(6)

Conclusion: Bipolar disorder (BD) is a relatively common chronic mood disorder that is characterized by cyclical periods of depression, mania/hypomania. According to the American College of Lifestyle (ACLM),

there are six essential pillars of medicine: lifestyle, diet, physical activity, avoiding substance use, stress management, adequate sleep, and social relations that affect BD.In this article, the relationship between sleep and bipolar disease is investigated.We found stronger relationships between sleep and hypomania in individuals with BD1 and stronger relationships of depression with insomnia in individuals with BD2. Also strong relationships adjusted for gender (strong relationships and sleep and hypomania for women and age (strong relationships) We found sleep and depression in young people.

Keywords: insomnia,bipolar disease,mania,depression,mood disorder

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The effect of intestinal microbes in Alzheimer's disease (Review)

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Introduction: Alzheimer's is a fatal degenerative brain disorder that leads to brain shrinkage and dementia. Alzheimer's disease is manifested by decreased levels of tau protein, hyperphosphorylation and accumulation of beta-amyloid peptide in the hippocampus and cingulate cortex. The nerve tissue of Alzheimer's patients contains fungal proteins that are associated with bacterial infections. Two methods of immunohistochemistry and next generation sequencing (NGS) were used to evaluate fungal and bacterial infections. The most common fungal species: Alternaria _ Candida _ Botris and Malassezia. Types of bacterial infection: Proteobacteria _ Actinobacteria _ Bacteroides Also, a sensitive cycle of uncontrolled neuroinflammation and neurodegeneration in the brain by herpes simplex virus type (HSV1)1. Systemic pro-inflammatory cytokines are produced by cytomegalovirus and Helicobacter pylori microorganisms. And then they can cross the blood and brain barrier and cause Alzheimer's disease. Inflammatory-activating gut bacteria release beta-amyloid protein and other neurotoxic substances. They can also secrete large amounts of amyloid and lyopolysaccharide. Bacteria produce endotoxin, which is usually found in the outer membrane of Gram-negative bacteria. During bacterial infection or changes in the metabolic processes of the intestinal microbiota due to inflammation, the concentration of LPS increases, which can cause neurodegeneration. Spirochetes contain amyloidogenic proteins and also induce beta amyloid deposition, tau protein phosphorylation, activate complement, affect vascular permeability, produce nitric oxide and free radicals, induce apoptosis. and are amyloidogens, which cause Alzheimer's disease.

Methods: Also microorganisms through the secretion of cortisol by the HPA in case of stress, which can affect intestinal motility, integrity, and mucus production, leading to changes in gut microbiota composition. This alteration, in turn, may affect the CNS through the modulation of stress hormones. Increased intestinal discomfort and altered BBB permeability cause microbiota dysbiosis, leading to the release of amyloids and lipopolysaccharides. This further modulates NF-κB signaling and a massive pro-inflammatory cytokine storm, causing neuronal loss.

Results: The mechanisms potentially involved in these processes as well as the potential of probiotics and prebiotics in therapeutic modulation of contributed pathways are discussed Through pro-inflammatory cytokines and chemokines.Immunity is also critically involved. Specifically, toll-like receptors (TLRs) and peptidoglycans (PGNs) mediate the immune response towards microbes by acting as sensors of microbial components. A local immune activation can, throughout different pathways, lead to an immune activation in different organs, including the brain. This low-grade immune activation has been implicated in the pathophysiology of some forms of depression and neurodegenerative disorders such as AD and Parkinson's disease (PD).

Conclusion: It can be said Nutrition is known to play an important role in the pathogenesis of Alzheimer's disease. Evidence is obtained that the gut microbiota is a key player in these processes. Dietary changes (both adverse and beneficial) may influence the microbiome composition, thereby affecting the gut-brain axis and the subsequent risk for Alzheimer's disease progression. In this review, the research findings that support the role of intestinal microbiota in connection between nutritional factors and the risk for Alzheimer's disease onset and progression are summarized.

Keywords: Alzheimer's disease , microorganism , Gut microbiota ,

The Effect of Ivermectin on HepG2 Cell Line Autophagy (Research Paper)

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Introduction: Hepatoma cell lines are commonly employed as in vitro substitutes for primary human hepatocytes. These cell lines possess enduring viability, a consistent phenotype, widespread accessibility, and straightforward manageability. HepG2, a human hepatoma cell line, finds frequent use in research related to drug metabolism and hepatotoxicity. These cells are non-tumorigenic, exhibit rapid proliferation, and display an epithelial-like appearance. Furthermore, they carry out various differentiated hepatic functions. Ivermectin has gained attention in cancer therapy due to its potential as an adjunct treatment in some cancer types. Preliminary studies have suggested that it might help inhibit the growth of certain cancer cells, although further research is needed to fully understand its efficacy and mechanisms in the context of cancer treatment. The present study aimed to study the effect of ivermectin on HepG2 autophagy.

Methods: HepG2 cells were cultured in DMEM medium containing 10% FBS and treated with 0.2, 0.4, 0.8, 1.5, and 8 µM concentration of ivermectin and 72 hours later were assessed for their viability by MTT assay. Giemsa staining and invert microscopy were used to evaluate the cell morphology. The expression of Beclin-1 and mTOR genes was evaluated by real-time PCR. Data analysis was performed using SPSS version 27.

Results: In the present study, IC50 of ivermectin on HepG2 was determined to be 0.4 µM. The highest effect was recorded on 8 µM concentration. The expression of Beclin-1 and mTOR was increased and reduced in PCR results.

Conclusion: The present study confirms the positive effect of ivermectin on HepG2 cancer cell autophagy. This could suggest the possible use of

ivermectin against liver cancer, however, more extensive studies are needed to prove its efficacy.

Keywords: Ivermectin, Autophagy, HepG2

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The Effect of Ivermectin On HT-29 Cells Apoptosis (Research Paper)

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Introduction: According to cancer statistics provided by the World Health Organization (WHO) and the International Agency for Research on Cancer (GLOBOCAN), cancer ranks as the second leading cause of death globally. Colorectal cancer is among the most frequent cancer types worldwide. Although cancer is more serious in the undeveloped and developing countries with low and mid gross domestic product (GDP), colorectal cancer has more incidence in developed countries. Ivermectin, primarily known as an anti-parasitic medication, is gaining attention for its potential role in cancer therapy. Research has shown that ivermectin may have anti-cancer properties by interfering with various cellular processes in cancer cells. It has been found to inhibit the growth and proliferation of cancer cells, induce programmed cell death (apoptosis), and interfere with cancer cell migration and invasion. The present study aims to assess the effect of ivermectin on the apoptosis of HT-29 cells, a major colorectal cancer cell line.

Methods: HT-29 cells were cultured in DMEM medium containing 10% FBS and treated with 0.2, 0.4, 0.8, 1.5, and 8 µM concentration of ivermectin and checked for their viability by MTT assay 72 hours later. To evaluate cell morphology, Giemsa staining and invert microscopy were used. Also, real-time PCR was incorporated to assess the expression of Bax, Bad, and Bcl-2 genes. All data were analyzed by SPSS version 27.

Results: IC50 of ivermectin on HT-29 cells was 0.8 µM. Maximum apoptotic effect was observed at 8µM eliminating 85% of HT-29 cells. Results of real-time PCR showed increased Bax and Bad and decreased Bcl-2 expression.

Conclusion: Based on the results of the present study, ivermectin can be a potential candidate in colorectal cancer cell treatment by inducing apoptosis in HT-29 cells. However, the clinical applicability of this finding should be assessed in further studies.

Keywords: HT-29, Apoptosis, Ivermectin

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The effect of Lactobacillus acidophilus probiotic on the oxidative stress induced by streptozotocin and aluminum chloride and the accumulation of this metal in blood and brain tissue. (Research Paper)

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Introduction: Heavy metals, including aluminum, are potentially harmful to human health and the environment. One of the severe effects of aluminum metal is the effect on the brain and memory impairment. Alzheimer's disease is the most common neurodegenerative disease that is associated with memory and cognition disorders, and the risk of it increases with age. Our country is facing middle age and it is very important to know the factors affecting age-related diseases. The present study has investigated the effect of Lactobacillus acidophilus probiotic on the accumulation of aluminum chloride in blood and brain tissue, as well as the oxidative stress caused by streptozotocin and aluminum chloride, either alone or simultaneously.

Methods: In this experimental study, adult male Wistar rats were divided into seven groups: control, streptozotocin (3 mg/kg) alone and with probiotic, aluminum chloride (0.8 g/L) alone and with probiotic, streptozotocin and aluminum chloride alone and with probiotics. In all experimental groups, cannulation was performed in the lateral ventricles. Animals received intracerebral injection of saline or streptozotocin on the first and third days after cannulation. Treatment with aluminum chloride and probiotics (with certain amount of turbidity) dissolved in drinking water was done from 1 day before cannulation until the beginning of experiments. At the end of the treatment Blood sampling was done from the right ventricle of the heart. Then, the level of malondialdehyde, total antioxidant power, activity level of superoxide dismutase and catalase enzymes in blood serum were measured. Aluminum levels were also measured in blood serum and brain tissue. Statistical analyzes were performed by SPSS software and the significance level was considered $p<0.05$.

Results: In animals that used drinking water containing aluminum chloride, the level of this pollutant in blood serum ($p<0.001$) and brain tissue ($p<0.001$) increased significantly compared to other groups. Also, drinking water containing aluminum chloride and intracerebral injection of streptozotocin each alone and simultaneously led to a significant decrease in total

antioxidant power ($p<0.001$), superoxide dismutase and catalase enzyme levels ($p<0.001$). And a significant increase in the level of malondialdehyde ($p>0.001$) was observed in the blood serum compared to the control group. While in all groups, the treatment of animals with Lactobacillus acidophilus probiotic leads to the reduction of aluminum chloride in the blood serum and brain tissue, as well as the improvement of oxidative stress factors to the level of the control group.

Conclusion: This research showed that aluminum chloride through drinking water is able to accumulate in the brain tissue and cause oxidative stress. The use of Lactobacillus acidophilus probiotic prevents the accumulation of aluminum chloride in the blood and brain tissue. Also, this probiotic is able to prevent oxidative stress caused by streptozotocin alone or together with aluminum chloride, so it is recommended to use probiotics in the diet.

Keywords: Aluminum chloride, Lactobacillus acidophilus, Memory, Diet, Streptozotocin.

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The effect of Lactobacillus ruteri supernatant on the replication of herpes virus type 1 and expression of UL54, UL52 and UL27 genes (Research Paper)

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Introduction: Herpes simplex virus type 1 (HSV-1) infection is a widespread and incurable viral disease in the human population with more than 90% of the individuals being seropositive to the pathogen. Due to increasing resistance to its primary drug, acyclovir, It is clinically significant to try alternative drugs with a different mode of action. Recently various lactic acid bacteria (LAB) and their post-metabolites have shown many antiviral effects. The aim of present study was to evaluate the effect of Lactobacillus ruteri supernatant on the replication of Herpes simplex virus type 1.

Methods: In this interventional study, The MTT assay was used to determine the possible cytotoxicity of the Lactobacillus ruteri supernatant. HeLa cells were treated with bacterial supernatant, and HSV-1 under pre-treatment (incubation of HeLa cells with bacterial supernatant then HSV-1 inoculation), pre-incubation (mixture of co-incubated HSV-1/bacterial supernatant added to HeLa cell), competition (adding HSV-1 and bacterial supernatant into HeLa cells simultaneously) and post-treatment (HeLa cells inoculated with HSV-1 then incubated with bacterial supernatant) assays. Viral titer reduction (TCID50) and expression of UL54, UL52, and UL27 genes by real-time PCR were measured in each experimental condition. t-student statistical test was used to evaluate the results.

Results: The results indicated that the HSV-1 titer under pre-treatment, pre-incubation, competition, and post-treatment decreased 0.42, 3.42, 1.83, and 0.83 Log10TCID50/mL respectively. Bacterial supernatant had the greatest reduction activity toward the expression of UL54, UL52, and UL27 genes in the pre-incubation assay. The expression of the genes did not show a significant decrease under post-treatment conditions.

Conclusion: The results indicated that the supernatant of Lactobacillus ruteri has a significant inhibitory effect on herpes simplex virus type 1 (HSV-1) replication under pre-incubation and competition circumstances. It could be considered a novel inhibitor for HSV-1 infection.

Keywords: Herpes Simplex Virus Type 1, Probiotic, Lactobacillus

The effect of lipids on Parkinson's disease (Review)

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Introduction: Parkinson's disease (PD) is a progressive and severe neurological disorder of the central nervous system. The main risk factors are age and environmental factors. This disease is more common in the elderly (over 60 years old). The reports of James Parkinson, an Italian surgeon, led to the identification of Parkinson's disease. The most obvious feature of this disease is the reduction of cells in several concentrated areas of the substantia nigra and the accumulation of alpha-synuclein protein and its increased concentration, especially in the brain stem, spinal cord, and cerebral cortex areas. This disease is caused by an imbalance between the basal ganglia as a result of dopamine inhibition of the putamen nucleus, which increases the inhibition of the thalamus, decreases the excitatory output of the thalamus, and causes movement disorders. Symptoms: Parkinson's disease is caused by less production of dopamine, a brain neurotransmitter in the neurons of the substantia nigra of the brain. Dopamine as a brain neurotransmitter is very important in another area of the brain called ganglia. This area of the brain is responsible for organizing the brain's commands for movement. Norepinephrine is reduced in people with Parkinson's disease. This chemical is effective in the functioning of the sympathetic nervous system. Its deficiency is associated with non-motor symptoms of Parkinson's. The movement symptoms of Parkinson's include: muscle stiffness, resting tremor, akinesia, bradykinesia, weakness in maintaining balance and reduction of unconscious and natural body movements. Non-motor symptoms of Parkinson's include: depression and anxiety, memory impairment, hallucinations and delusions, swallowing and chewing disorders, urinary problems and sleep disorders. Effect of lipids in disease: Lipids are biomolecules that are soluble in organic and non-polar solvents and are considered as components of biological membranes. Different groups of fat can play a role in Parkinson's disease. Research shows that changing the structure of fatty acids and replacing long-chain unsaturated acids with saturated fatty acids, phosphatidylcholine, phosphatidyl-inositol, phosphatidyl-serine, cholesterol, ganglioside, cerebroside, and sphingolipids are effective in PD. Alpha-synuclein (AS) is a small protein that is abundantly expressed in the brain, but is mainly located in the synaptic terminal. After binding to the membrane, this protein is effective in synaptic plasticity. Normally, after AS protein binds to the membrane, the initial 95 residues of this protein undergo a

conformational transition. In this case, it turns from a random coil to a helix. Changes in the nature and chemical properties of lipids lead to the tendency of AS protein to aggregate, leading to cytotoxicity. Recent studies suggest that this synucleopathy may be a protein-induced lipidopathy. Indeed, an imbalance in cellular lipid homeostasis creates a process that leads to fibrillar aggregation of AS protein. In fact, lipidopathy and proteinopathy simultaneously cause the symptoms of this disease.

Methods: Animal studies on Parkinson's disease have shown that lipid damage is effective in the occurrence of the disease. Animal models showed that changes in lipids affect dopaminergic neurons and glial cells. This effect is especially on microglia and astrocytes and is associated with accumulation of alpha-synuclein protein in dopaminergic neurons. which itself causes vulnerability in the disease process. Triglyceride lipid levels are also associated with an inflammatory marker in the brain. Examining animal models showed that changes in a specific cell in the brain can lead to Parkinson's disease.

Results: Classically, PD was thought to be a lipid-mediated proteinopathy. In this hypothesis, the incorrect folding of this protein in the form of B-Sheet leads to the accumulation of this protein in Lewy bodies and causes an imbalance in protein folding and destruction, and ultimately leads to neurological disorder and death due to the oligomerization of this protein. But new investigations in Lewy bodies and animal models showed that this synucleopathy may be protein-induced lipidopathy.

Conclusion: Changes in the content of lipids have far-reaching consequences in the field of normal nerve and brain function. The composition of lipid content is not only related to the genes involved in lipid metabolism, but endogenous factors such as food fats, lifestyle, sleep patterns, drug effects and food selection are also effective in it. To validate these studies, the relationship between lipids and Parkinson's disease is needed to help identify biomarkers and develop drug targets and treatments.

Keywords: Parkinson's disease, dopamine, norepinephrine, lipids, alpha-synuclein protein

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The effect of lithium and exercise on the expression levels of mitochondrial genes (PGC1 and SIRT3) in the muscle of the Wistar rat: the role of BDNF protein (Research Paper)

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Introduction: Skeletal muscle is responsible for consuming a significant portion of the body's energy supply, accounting for roughly 40% of a healthy individual's body mass. In response to the stress of contractile activity, skeletal muscle undergoes changes in gene expression that lead to increased expression of cytoprotective proteins. peroxisome proliferator-activated receptor γ coactivator α (PGC-1α) and SIRT3 play a critical role in coordinating the activation of genes required for mitochondrial biogenesis in skeletal muscle. Lithium is primarily indicated for the treatment of bipolar disorder, however, the positive effects of lithium on mitochondrial activity were also observed in in vivo. BDNF may be a contributing factor to the some of effects of lithium. The present study aims to examine the gene expression of SIRT3, PGC1-α, and BDNF enzyme following a 6-week moderate-intensity training and lithium intervention in 42 Wistar rats. It is hypothesized that this intervention will increase the levels of proteins associated with mitochondrial function.

Methods: In this research, 28 male Wistar rats were divided into 4 groups; I: Control (Crt), animals did not receive drug; II: Li10 (10 mg/kg/day/ip); III: Moderate-intensity training (MIT); IV: Li10 and MIT (Li10+ MIT). Moreover, the density of BDNF (brain-derived neurotrophic factor) was assessed by the ELIZA method.

Results: Our data showed the positive effects of MIT and lithium on the expression of the PGC1 gene, however, the combination of MIT and lithium had opposite effects. The mRNA level of the SIRT3 gene in the studied groups was different compared to the PGC1 gene. Finally, we observed a positive role of BDNF protein in the exercise and lithium effects.

Conclusion: Our data showed the positive effects of MIT and lithium on the expression of the PGC1 gene, however, the combination of MIT and lithium had opposite effects. The mRNA level of the SIRT3 gene in the studied groups was different compared to the PGC1 gene. Finally, we observed a positive role of BDNF protein in the exercise and lithium effects.

Keywords: Moderate-intensity training, lithium, PGC1, SIRT3

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The effect of lithium and exercise on the spatial learning and memory in the Wistar rats: the role of BDNF protein (Research Paper)

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Introduction: Lithium has been found to have neuroprotective properties and can improve memory and learning in preclinical models of aging, traumatic brain injury, drug addiction, glutamate neurotoxicity, and Alzheimer's disease. Regular physical exercise (EX) is considered to be the most powerful non-pharmacological approach for promoting optimal brain health. Given the findings of previous research, it is hypothesized that moderate-intensity exercise and lithium treatments could promote improvements in spatial learning and memory in Wistar rats by activating brain-derived neurotrophic factor (BDNF) in the hippocampus. This study evaluated the role of BDNF in the effects of lithium and exercise on spatial learning and memory.

Methods: In this research, 28 male Wistar rats were divided into 4 groups; I: Control (Crt), animals did not receive drug; II: Li10 (10 mg/kg/day/ip); III: Moderate-intensity training (MIT); IV: Li10 and MIT (Li10+ MIT); One hour after the last injection, the Morris water maze (MWM) test was conducted. Moreover, the density of BDNF (brain-derived neurotrophic factor) was assessed by the ELIZA method.

Results: Our result showed the beneficial effects of exercise on spatial learning and memory; however, lithium administration alone cannot affect this. Additionally, exercise-exposed and lithium administration combined rats showed improvement in spatial learning and memory. Finally, we observed a positive role of BDNF protein in the exercise and lithium effects.

Conclusion: lithium or MIT separately affected the expression of the mitochondrial gene positively, however, combined lithium and MIT showed different effects. The BDNF protein has a positive role in the exercise and lithium effects.

Keywords: Lithium, exercise, MWM, BDNF

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The Effect of Midwifery-Led Supportive Program on Coping Strategies and Stress in Breast Cancer Women: A Randomized Controlled Clinical Trial (Research Paper)

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Introduction: Breast cancer is the most common cancer in women accounting for 33% of all types of cancer and 19% of deaths caused by cancer in women. Its diagnosis and treatment are one of the sources of stress and crisis in women's lives. Coping strategies are one of the effective mechanisms to help breast cancer patients; as these patients need help to adopt their disease, effectively, and encounter with it correctly. Breast cancer women have more psychological problems and need to some interventions to cope with these problems. This study aims to determining the effect of midwifery-led supportive program on coping strategies and stress in breast cancer women.

Methods: This randomized controlled clinical trial was conducted on the breast cancer women referring to the outpatient chemotherapy ward of Imam Khomeini Hospital in Sari during 2018. Therefore, permuted block randomization method was used to assign 60 cases into two groups of intervention (n=30) and control (n=30). Six 90-mintue intervention sessions were held weekly. Instruments of the study included sociodemographic and clinical characteristics, Ways of Coping Questionnaire, Depression-Anxiety-Stress Questionnaire, Medical Outcomes Study Social Support Survey and the Religious Attitude Scale Revised, which were completed by the patients

before, immediately, and one month after the intervention for follow-up. Data were analyzed with SPSS -18.

Results: The score of the problem-focused coping strategies increased 17.12 in the intervention group comparing the control group (P<0.001). Moreover, the scores of emotion-focused coping strategies and Stress decreased 7.84 score and 4.89 score in the intervention group comparing to the control group (P<0.001).

Conclusion: According to the effectiveness of the midwifery-led supportive program on the enhancing coping strategies and reducing stress in breast cancer women, it is recommended to promote the health of women with breast cancer by informing oncologists, surgeons, and patients about non-pharmaceutical methods, including the midwifery-led supportive program and give the patients a choice to choose these methods beside empowering the health care providers.

Keywords: Breast cancer, coping strategies, stress, supportive program, midwifery-led care

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The Effect of Nutritional Status on Intestinal Parasitic Infections in Primary School Students in Tehran (Research Paper)

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Introduction: Parasitic infections in children can affect their growth, health, nutritional status and cognitive development. The aim of this study was to evaluate intestinal parasitic infections and their relationship with the nutritional status of primary school students in Tehran in 2020.

Methods: The current study was conducted on 250 samples collected by the available sampling method from two selected residential settlements in Tehran. For all samples, in addition to the direct test method, the formalin-ether concentration method (Sedimentation method) was used. The Mini Nutritional Assessment (MNA) questionnaire was used to assess nutritional status. The collected data were entered into SPSS 23 and descriptive statistics were performed using the Chi-square statistical test. A significance level of 0.05 was considered.

Results: Out of 250 samples collected from students, 40 cases had a parasitic infection. In terms of nutrition, 18 cases were malnourished, 212 cases were exposed to malnutrition, 20 cases had normal nutrition, and there was a significant relationship between parasitic infection and malnutrition ($p<0/05$); Also, there was a significant correlation between parasitic infection and malnutrition in children and the level of education of their parents. It seems that some pathogenic parasites are still common in the region and should be carefully monitored.

Conclusion: Our findings showed that parasitic infection is associated with malnutrition in children; therefore, raising health awareness in the field of individual health and nutrition among students and parents is essential.

Keywords: Parasitic infection, Malnutrition, Children.

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The effect of parenting styles on children's health: A review study (Review)

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Introduction: Parenting styles as one of the important principles in raising children have an important role in the health of later life. This study was conducted to review the effect of parenting styles on children's health.

Methods: This study was a review method. Gather information in the databases of SID, Pub Med, Scopus, Google scholar, Web of Science and search with the keywords "Children's health", "Parenting styles" and "Effective interventions", their Persian equivalent in the period 2005 to 2023. At the end of the 73 articles searched, 17 articles related to the purpose were reviewed.

Results: The results of the present study show, Powerful style will enhance the mental health (reduction of depression and identity crisis in adolescence, secure attachment), social health (independence, reduction of destructive and high social risk behaviors) and physical health (reduction of enuresis) in children. Careless and authoritarian parenting style can lead to negative effects on mental health (mood disorders and hyperactivity), social health (increased risk of risky behaviors) and physical health (increased incidence of enuresis) in the short term and Be long-term.

Conclusion: It seems that children's health is not a one-dimensional matter and parenting style is one of the important factors in it.Authoritative style is the most appropriate method of parenting and leads to the formation of healthier behaviors and characteristics in children.

Keywords: Parenting Styles, Children's Health, Parents' Health.

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The Effect of platelet-rich plasma (PRP) on the improvement of pregnancy outcomes in patients with repeated IVF failure: A Review Article (Review)

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Introduction: More than four decades of use of assisted reproductive technology (ART) have passed around the worldwide, But more than 60% of women undergoing in vitro fertilization (IVF) treatments fail to become pregnant after the first embryo transfer and nearly 20% of patients are suffering from unexplained recurrent implantation failures (RIFs) and repeated pregnancy loss (RPL). The studies have reported different causes of RIF-RPL, mainly multifactorial, endometrial and idiopathic. Platelet-rich plasma (PRP), which represents a valuable source of growth factors, is increasingly being applied in human reproductive medicine. Recent findings suggest the feasibility of using PRP in the treatment of infertility secondary to refractory thin endometrium. Indications for PRP therapy show its positive effects in promoting endometrial and follicular growth and gestation in assisted reproduction cycles, as has been proven in animals. This review studyaimed to determine the effect of platelet-rich plasma (PRP) on the improvement of pregnancy outcomes in patients with repeated IVF failure.

Methods: In order to investigate effect PRP on the improvement of pregnancy outcomes in patients with repeated IVF failure which have been studied to date, keywords including Platelet-rich plasma (PRP) and In Vitro Fertilisation(IVF) was searched in the following databases: ISI, Pub Med, Science direct, Google Scholar, Scopus, Science direct, Iran medex and Magiran from 2019 to 2023 and 27 papers were evaluated.

Results: RIF has remained a black box because of the complicated categorization and causes of this physio-pathological dysregulation of implantation and pregnancy process after ovarian stimulation but endometrial thickness has been identified as a prognostic factor for pregnancy rate for patients with female infertility. Thin endometrium is defined as <7 mm on the day of ovulation, during in vitro fertilization (IVF) cycles. Many options were suggested as solutions for improving the endometrial thickness and embryo implantation rate of the patients with thin endometirum and in order to treat RIF-RPL with controversial results on their usefulness and and clinical outcomes. One of these options is PRP that applications in human

reproductive medicine are recent, and the role of platelet growth factors in improving the endometrial environment is well known. Indications for PRP therapy show its positive effects in promoting endometrial and follicular growth and gestation in assisted reproduction cycles. . Some randomized controlled trials have reported the application of PRP for patients with thin endometrium with satisfactory effect. So that could effectively improve uterine proliferation, markedly accelerate endometrial damage repairment and increase the fertility ratein in failures following IVF.

Conclusion: According to studies, PRP can be a promising therapeutic solution in patients with RIF-RPL and be effective in improving pregnancy outcomes.

Keywords: Platelet-rich plasma (PRP) - Pregnancy -In Vitro Fertilisation(IVF)

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The effect of probiotics on the response of triple negative breast cancer to immunotherapy (Review)

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Introduction: The absence of HER2, estrogen receptors, and progesterone receptors distinguishes the aggressive subtype of breast cancer known as triple-negative breast cancer (TNBC). TNBC has fewer therapy choices than other forms of invasive breast cancer because of this. Because a variety of therapeutic approaches, including hormone therapy, rely on the expression of the aforementioned receptors. TNBC can currently be treated successfully with immunotherapy techniques such as targeted monoclonal antibodies, natural killer cell therapy, and therapeutic cancer vaccines. Immunotherapy response rates in TNBC patients, however, continue to be below average, necessitating the development of methods to increase its efficacy. Live microorganisms known as probiotics that help the host's health have drawn interest due to possible immunomodulatory effects. Probiotics may have an impact on the tumor microenvironment and immune response, according to several studies, which raises the possibility that they could boost the effectiveness of TNBC immunotherapy. The purpose of this review is to assess how probiotics affect TNBC's immunotherapy response.

Methods: A review has been written for this article. Based on keywords and their synonyms, a specific search strategy was chosen. Following that searches in the Google Scholar and PubMed databases were used to retrieve the articles. Only primary studies, including interventional and observational ones, were examined. Keywords included probiotics, TNBC and immunotherapy. The collected publications were examined subjectively and filtered based on predetermined inclusion and exclusion criteria. The results of the chosen articles were then given, along with the study's methodology and key findings.

Results: Probiotics may help TNBC patients respond more favorably to immunotherapy, according to preliminary research. Probiotics work by increasing anti-tumor immune responses, lowering immunosuppressive factors, altering the composition of the gut microbiota, and improving the effectiveness of cancer vaccinations. Probiotics can enhance the effectiveness of immunotherapy in this way as an adjuvant therapy that is simple to administer and has few side effects.

Conclusion: Developing individualized treatment plans requires an understanding of how probiotics affect TNBC's response to immunotherapy. Utilizing probiotics as an additional therapy may provide a cutting-edge method to boost immunotherapy effectiveness, ultimately leading to better outcomes for TNBC patients. The discovery of novel therapeutic strategies for TNBC and perhaps other malignancies is possible with more research in this area. To clarify the underlying mechanisms and identify ideal probiotic formulations and treatment plans for TNBC patients, additional research is necessary.

Keywords: Probiotics - triple negative breast cancer - immunotherapy

The effect of recombinant drugs on cancer (Review)

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Introduction: Cancer is one of the deadlyest diseases in the world. Common cancer treatments such as chemotherapy and radiation therapy have a low survival rate, which is due to tumor progression, resistance to treatment, and non-specificity of treatment for the tumor. The production of recombinant proteins is one of the most important achievements of biotechnology in the 20th century. Using the natural power of prokaryotic and eukaryotic host cells to express recombinant proteins has led to the development of multi-billion dollar industries. Recombinant proteins have become very important for medical applications Bacteria can specifically target tumors, actively penetrate and search the tissue, and produce toxicity in a controlled manner. Cancer is one of the deadliest diseases worldwide. Common cancer treatments such as chemotherapy And radiation therapy has a low survival rate, which is due to tumor progression, resistance to treatment, and non-specificity of treatment for the tumor. Bacteria can specifically target tumors, actively infiltrate and search the tissue, and produce toxicity in a controlled manner.

Methods: Based on the studies that have been conducted and the articles that have been studied, it can be found that bacteria can specifically target tumors, actively penetrate and search the tissue, and create toxicity .in a controlled manner The toxin causes red blood cell lysis with a time-dependent process; Non-lethal concentrations of the recombinant toxin FraC caused a 4- to 6-fold increase in the lethal effects of the drug 5-fluorouracil at .different times of action on MCF-7 cell

Results: Expression of the recombinant FraC protein 21 BL bacterial colonies containing pET28a-FraC expression vector were cultured in LB culture medium containing the antibiotic kanamycin, and by adding IPTG to a concentration of 100 µM and passing at least 3 hours, the bacterial pellet was collected and in a SDS-PAGE gel. , the protein content of the bacteria containing the expression vector was compared before and after the induction of protein expression The toxin causes red blood cell lysis with a time-

dependent process. In this study, histidine tag is attached to the toxin gene at the carboxyl terminus for protein purification. It seems that this work did not have an inhibitory effect on the biological activity of the toxin. The survival rate of MCF-7 cells in the presence of FraC recombinant toxin. trypan blue assay were tested. As can be seen in Figure 6, at 24 and 48 hours, there is a significant difference in the effect of the drug Fl5 and rivuracil on cells in the presence and absence of the recombinant toxin. The values of 50 ICs obtained with Graphpad software are summarized in Table 1. As it is clear, the non-lethal concentrations of the recombinant toxin FraC caused a 4 to 6 fold increase in the lethal effects of the drug 5-fluorouracil at different times of action on MCF-7 cells.s

Conclusion: Cancer treatment faces major challenges, including the lack of specific of treatment methods. It has been widely observed that chemotherapy or radiotherapy cause significant side effects. The non-specific targeting and the toxicity of the own cells limit the effectiveness of the treatment. Therefore, recent research efforts have been focused on the treatment of cancer by biological molecules, recombinant proteins, especially antibodies and targeting peptides, as well as other specific agents such as aptamers.

Keywords: Cancer,Recombinant medicine, Chemotherapy,Toxin

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The effect of recombinant nanomedicine of 5-fluorouracil and sodium butyrate on microRNA let7 on mcf7 breast cancer cell line (Research Paper)

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Introduction: The treatment for certain cancers requires the use of recombinant drugs. The majority of patients eventually acquire treatment resistance, and new mutations render old treatments ineffective, as a result of our glacial pace in designing and executing clinical trials for effective medications and the tsunami-grow like development of cancer. The aim of this study was to enhance one of the drugs that caused significant resistance in individuals with breast cancer and combine it with another component in ordering to increase its efficacy.

Methods: The effects of sodium butyrate and 5-fluorouracil nanomedicine on the mcf7 cell line were investigated with a focus on Mir Let7 using MTT assay and real-time PCR. The cells were exposed to nanomedicine using the MTT method for 24, 48, and 72 hours, and then the Real-time PCR method was used to assess the expression level

Results: Previous research has identified Mir-let7 as one of the breast cancer indicators. This microRNA functions as a tumor suppressor in the cell, inhibiting tumor cell migration and proliferation as well as decreasing the expression of Mir let7 in these cells.

Conclusion: The outcomes demonstrated a notable dose-dependent increase in miR-let7.

Keywords: 5fu,Sodium Butyrate ,MirLet7 ,Mcf7, 5Fluorouracil

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The effect of three commonly used antibiotics amoxicillin, cefixime and metronidazole on the abundance of microorganisms in soils with different concentrations of heavy metals (Research Paper)

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Introduction: It has been clarified that the simultaneous toxic effect of antibiotic and heavy metal on microorganisms is higher than their separate effect. On the other hand, the simultaneous pollution of antibiotics and heavy metals increases antibiotic resistance genes, bacterial resistant and horizontal transfer of antibiotic resistance genes and has consequences on the diversity and abundance of microorganisms. On the other hand, reports show that more than 50% of lands around the world are contaminated with heavy metals (Lormohammadi et al., 2022; Yang et al., 2022; Zhou et al., 2022). Therefore, the transformation of the soil microorganism community against metal and antibiotics pollution is the main goal of this research, in which to investigate the frequency of some soil microorganisms in response to the application of three antibiotics amoxicillin, cefixime and metronidazole in three soils: agricultural, rangeland soil and mining wastes with amounts various heavy metals were collected from Hamadan city. Therefore, the changes in the abundance of fungi and bacteria and the special group of enterobacteria and Pseudomonas in the treatment of the mentioned antibiotics were investigated in these soils. The findings of this research show the difference between groups of microorganisms and how they metabolize in response to the mentioned antibiotics, which can be used in selecting the treatment method for people and livestock, as well as the stability of microorganisms in different habitats.

Methods: Three soil samples were selected from mining wastes, rangeland and agricultural soil then concentrations of 100 and 200 mg.kg-1 antibiotics were applied to the soils. In three time periods: 0 to 7 days (short-time incubation), 15 and 30 days (medium-time), 60 and 90 days (long-time), the abundance of four groups of soil microorganisms (fungi, bacteria, pseudomonas and enterobacteria) was counted. Factorial experiment was performed with a completely randomized design in three replications.

Results: Data analysis showed that in the short time, the abundance of four groups of microorganisms in agricultural soil decreased in amoxicillin treatment (up to 5.92 percent) but were more resistant in contaminated mine and rangeland soils and increased to 11.91 % against their control. The fungi of two mine and rangeland soils against amoxicillin decreased to 6.73 %. Also in this period, the population of all microorganisms in rangeland soil and agricultural soil (except agricultural pseudomonas) decreased to 11.52 % and also bacteria and pseudomonas of mining soil against Cefixime decreased to 13.5 %. At start up to 7 days of incubation, mine soil bacteria, pseudomonas of agricultural soil and enterobacteria of two agricultural and rangeland soils showed resistance against metronidazole. The data analysis showed that the long-time use of all three antibiotics in rangeland and mine soils led to a positive response in the abundance of all bacteria, pseudomonas and enterobacteria in the soil compared to the control treatment. On the other hand, it should be said that the addition of antibiotics to soils with high concentrations of heavy metals can increase the abundance of enterobacteria in the soil. In agricultural soil, at the end of 90 days of incubation, the abundance response of all bacteria, pseudomonas, fungi and enterobacteria to the application of all three antibiotics was negative. In the long-time period, the lowest number of enterobacteria was obtained with the use of 200 mg. kg-1 metronidazole and the lowest number of pseudomonas with the use of 200 mg. kg-1 amoxicillin. Amoxicillin (200 mg. kg-1) showed the lowest number of fungi in medium-time incubation. The bad effect of 200 mg concentration of metronidazole on the abundance of microorganisms was intensified in the high concentration of heavy metals in the soil.

Conclusion: The response of microorganisms in different soils to each of the used antibiotics is not the same. Although the abundance of microorganisms in soils contaminated with heavy metals is less, but their ability to live against antibiotics is higher. Overall, the resistance of bacteria in metal-contaminated soils was higher against antibiotics, and the harmful consequences of antibiotics in the medium and long time, especially in soils contaminated with heavy metals (rangeland and mine) disappeared.

Keywords: Amoxicillin, Cefixime, Heavy metals, Metronidazole, Population of Soil Microorganisms

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The effect of Thymus vulgaris (Thyme) on cancer (Review)

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Introduction: Cancer is one of the life-threatening diseases which creates major problem in both the developing and developed countries. Demand for new methods to prevent this disease is growing increasingly. Plants have always been a basis for the traditional medicine systems and they have provided continuous remedies to the mankind for thousands of years. Medicinal plants are considered as a repository of various bioactive compounds and used for long time due to its therapeutic properties. Plant derived product has benefits over synthetic medicine which increased the utilization of medicinal plants in the healthcare sector as several plants' derived compounds show potential role against cancer treatment. Thymus vulgaris (Thyme), which is a medicinal plant, has pharmacological activities that include antibacterial, antioxidant, anti-inflammatory, antiviral and anti-cancerous activities.

Methods: We searched the keywords "Thymus vulgaris and Cancer" and "Thyme and Cancer" on PubMed and Google Scholar databases and collected articles related to these topics and after reading them, we wrote this review article.

Results: Several researches have been conducted on the effect of Thymus vulgaris (Thyme) on various cancers, including colorectal, breast, lung, head and neck cancer, etc. By studying the effect of this plant on cancers, researchers reached remarkable results.

Conclusion: According to the research done, it can be said that Thymus vulgaris (Thyme) has an effect on various cancers and is also known as an anti-cancer plant.

Keywords: Thymus vulgaris, cancer, Thyme

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The Effect of Triclabendazole on The Apoptosis of HepG2 Cell Line (Research Paper)

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Introduction: Being one of the leading causes of cancer-related mortalities worldwide and ranking as the fifth most prevalent in the United States, liver cancer stands as the sole member among the top five deadliest cancers to exhibit an annual rise in its occurrence rate. Liver diseases are more prevalent in developing nations. Triclabendazole, categorized as a novel imidazole compound, has gained FDA approval for the management of fascioliasis. Its actions involve, in part, processes associated with apoptosis. It has been showed that triclabendazole triggers apoptosis by controlling the levels of apoptotic proteins like Bax and Bcl-2, leading to increased cleavage of caspase-8/9/3/7 and PARP. Furthermore, it also promotes the cleavage of GSDME. This study aimed to study the effect of triclabendazole on the apoptosis of HepG2 cells.

Methods: Liver cancer cell line, HepG2, were cultured in complete DMEM (containing 10% FBS, 100 IU/ml penicillin, 100 µg/ml streptomycin, and 2 mM L-glutamine) and treated with 20, 40, 80, 160, and 320 µM concentration of triclabendazole. After 72 hours, they were evaluated for their viability by MTT assay. Giemsa staining and invert microscopy were used to study morphology. Also, real-time PCR was used to assess the expression of apoptotic genes Bax, Bad, and Bcl-2. Data analysis was done by SPSS version 27.

Results: IC50 of triclabendazole was determined to be 80 µM. The highest apoptotic effect was observed at 320 µM eliminating 92% of all HepG2 cells.

Real-time PCR results showed an elevation in the expression of Bax and Bad genes and Bcl-2 gene were suppressed and reduced.

Conclusion: Based on the results of the present study, triclabendazole could be considered as an anticancer agent in cancer treatment process. However, this concept is still new in literature and more studies are needed to prove its applicability.

Keywords: Triclabendazole, Apoptosis, HepG2

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The effect of zinc and L-arginine supplementation on height increase in children (Review)

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Introduction: Children's short stature is one of the primary manifestations of nutritional status and an indicator of chronic malnutrition, which can cause complications such as the occurrence of diseases, early death, reduced mental development and functional weakness of children. Inadequate child nutrition and lack of nutrients is one of the most important causes of growth defects in these children. Among the nutrients, zinc and protein have a significant effect on the bone and muscle growth of the body in terms of both quantity and quality. L-arginine is an essential amino acid for children that the body cannot make naturally. L-arginine can increase the height of children by increasing the secretion of growth hormone. Zinc element is effective in bone growth and height increase by affecting the secretion of some hormones and also by increasing the production of vitamin D and as a result calcium absorption. On the other hand, by influencing the activity of somatomedin hormone, which is stimulated by the secretion of growth hormone, zinc creates cartilage and bone tissue and is an effective factor in the growth of the body and the growth of the bone skeleton.

Methods: The present study is a review of the articles registered in PubMed, SCOPUS, Embase, ProQuest and Google Scholar sites until 2019. The inclusion criteria included: 1) clinical trial studies, 2) human studies, 3) studies in English, and cell studies, reviews, animal studies, letters to the editor, and articles in non-English language were excluded from the study. These articles have investigated the effect of L-arginine and zinc supplements on children's growth.

Results: After searching the database, the title and abstract of 402 studies were examined and finally 10 eligible studies were considered. The results of 3 reviewed studies showed that the effect of daily L-arginine supplementation is effective on increasing the height of children. In 8 studies, the positive effect of zinc and L-arginine supplementation on height growth was found, and in 2 studies, contradictory results were seen.

Conclusion: The results of the review of the articles showed that the daily supplement of 1 mg of zinc per kilogram of body weight and 3 grams of l-arginine per day is recommended in short children to improve height growth.

Keywords: Zinc,L-arginine, supplementation, height increase, children

The Effectiveness of Mobile Health in the Management of Oral Cancer Patients: A Systematic Review (Review)

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Introduction: Oral cancer is one of the most common types of cancer with dangerous consequences. Nowadays, screening and early detection of oral cancer is possible with the use of mobile health. Therefore, the present systematic review was conducted to evaluate the effectiveness of mobile health on the management of oral cancer patients.

Methods: The present study follows the PRISMA guidelines to investigate the effectiveness of mobile health on the management of patients with oral cancer. For this purpose, PubMed, Scopus and Web of Science databases were searched to retrieve English articles without time limit and until September 25, 2022. The search strategy included the terms "Mobile health", "Oral cancer" and their synonyms. The inclusion criteria in the study were original and English articles that were carried out with the aim of evaluating the "the effectiveness of the use of mobile health on the management of oral cancer patients". After selecting the studies, considering the inclusion and exclusion criteria, data collection was done using the data extraction form based on the study objectives. Data analysis was done through content analysis method.

Results: In the initial review of the three databases, 168 articles were retrieved and entered into the Endnote software. After removing duplicates (84 articles) and unrelated ones based on evaluation of title and abstract (33 articles), and full text (28 articles), finally 23 articles remained. 70% of mobile health interventions were used for diagnosis, 18% for risk assessment, 4% for treatment, 4% for surveillance and 4% for follow-up of the patient. The methods used to manage oral cancer included mobile phone application (62%), artificial intelligence algorithms (30%), SMS service (4%), and tablet-based microscope (4%). The target population included oral cancer patients

and people with oral lesions (48%), normal and high-risk population (40%), physicians (4%) and treated people (4%), and the target population was not mentioned in 4% of articles. 96% of the studies indicated the success of mobile health in improving the management of oral cancer, while in 4% of the studies, the use of mobile health did not make a difference in the process of disease management.

Conclusion: The review of articles showed that mobile health has an effective role in the management of oral cancer. Various interventions and services necessary for oral cancer patients can be performed remotely. Therefore, it is suggested to use mobile health capabilities to provide services to patients more broadly.

Keywords: Mobile health, mobile app, oral cancer, mouth neoplasm

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the effectiveness of synthesized zink/iron oxide nana composites by single-stage sol-gel method on anxiety , spatial learning and memory in rats exposed to noise stress (Review)

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Introduction: Nanotechnology is one of the interdisciplinary researches that has opened a new window of wonder in the world of science and knowledge. Nanotechnology, relying on the properties of nanoparticles in the field of diagnosis and treatment, has presented a clear perspective to researchers. Interdisciplinary collaborations of scientists and researchers in convergent sciences (NBIC) including science and nanotechnology, biotechnology, information technology and cognitive science can answer many questions and human needs, including in the field of prevention and treatment, by studying the brain and its functions. Nanoparticles cause environmental pollution in various fields. Due to the high permeability of nanoparticles, they easily pass through the blood-brain barrier (BBB), so it is possible that these substances may cause unwanted side effects. On the other hand, passing these substances through the blood-brain barrier and reaching the hippocampus can have destructive or improving effects on stress, anxiety and improving learning and spatial memory, which are among the very important concepts in psychology that deal with these issues. And the discovery of its unknowns will be of great help to the development of psychological science and the improvement of strategies to strengthen memory and reduce stress and anxiety. With the first industrial revolution, the entry of noise stressors into the work environment and human life increased. With the expansion of the use of nanotechnology, it seems necessary to study the harmful or beneficial effects of nanoparticles on neuropsychological mechanisms. Researchers of biological psychology and physiology and nanotechnology should enter this interdisciplinary field in order to be able to determine the necessary good news and warnings in the field of the use of these nanomaterials and its synergistic effects with environmental stresses on the physical and mental health of people along with the emergence of new technologies. do The aim of this study is to investigate the effect of exposure to noise pollution caused by traffic in rats on the neuronal activity of this area of their hippocampus and its effect on anxiety, learning and spatial memory along with the administration of zinc/iron oxide nanocomposites, which according to our studies, so far No research has been done in the field. With the first industrial revolution, the entry of sound stressors into the working environment and

human life increased, and with the expansion of the use of nanotechnology, studying the harmful or beneficial effects of nanoparticles on neuropsychological mechanisms seems necessary. Researchers of biological psychology and physiology and nanotechnology should enter this interdisciplinary field in order to be able to determine the necessary good news and warnings in the field of the use of these nanomaterials and its synergistic effects with environmental stresses on the physical and mental health of people along with the emergence of new technologies. do The aim of this study is to investigate the effect of exposure to noise pollution caused by traffic in rats on the neuronal activity of this area of their hippocampus and its effect on anxiety, learning, and spatial memory along with the administration of zinc/iron oxide nanocomposites, which according to our studies, so far No research has been done in the field. The mechanism of LTP in the hippocampus region can be evaluated and investigated as the most important region involved in memory formation and learning.

Methods: In this research, the effectiveness of zinc/iron oxide nanocomposites on anxiety, learning, and spatial memory in rats exposed to sound stress was investigated. First, zinc/iron oxide nanocomposites were prepared by the one-step sol-gel method. Then, it was characterized using SEM and transmission electron microscope, as well as XRD. In the continuation of this study, 8 groups and each group with 10 mice included, control group, stress group, control groups receiving nano including three doses of zinc/iron oxide nanocomposites (5, 2.5, 1.25 mg/kg) and The groups receiving nano stress which included three doses of nanocomposite were investigated. After 15 days, in order to investigate anxiety, learning and spatial memory, elevated plus maze test, Morris blue maze and electrophysiological recording of the Schafer collaterals pathway of the hippocampus were used. The results show that zinc/iron oxide nanocomposites did not have an ameliorating effect on anxiety in the elevated plus maze test and did not affect learning in the Morris blue maze test and did not have a positive effect on the animals' memory in the probe phase. On the other hand, the injection of zinc/iron oxide nanocomposite to the animals subjected to sound stress improved the induction of LTP in them, while the injection of nanocomposite had a negative effect on the induction of LTP in the animals of the control group. Determining the exact mechanism of the effect of zinc/iron oxide nanocomposite on improving or destroying memory requires additional tests. In this study, 80 adult male Wistar rats weighing about 220-250 grams were used, which were randomly divided into 8 groups of 10. The animals were kept in the animal house with an approximate temperature of 25°C and a humidity level of 55%, under conditions of 12 hours of darkness and 12 hours of light, and they had easy access to standard food and water. The sampling method was performed as a simple random one-step method. The studied

groups are as follows: 1- The control group that does not receive zinc/iron oxide nanocomposite and does not face noise pollution (CO). 2- The group of rats that received zinc/iron oxide nanocomposite in the amount of (5 mg/kg) for 12 days but did not face noise pollution (CO+N5). 3- The group of rats that received zinc/iron oxide nanocomposite in the amount of (5.2 mg/kg) for 12 days but did not face noise pollution (CO+N2.5). 4- The group of rats that received zinc/iron oxide nanocomposite in the amount of (25.1 mg/kg) for 12 days but did not face noise pollution (CO+N1.25). 5- Stress group; Rats exposed to noise pollution for 2 hours between 8:00 AM and 12:00 PM for 12 days and received normal saline (ST). 6- Rats are exposed to noise pollution for 2 hours between 8 am and 12 noon for 12 days and receive zinc/iron oxide nanocomposite in the amount of (5 mg/kg) from the beginning of stress to conducting electrophysiology tests. (ST+N5). 7- Rats are exposed to noise pollution for 2 hours between 8:00 AM and 12:00 PM for 12 days, and receive zinc/iron oxide nanocomposite in the amount of (5.2 mg/kg) from the beginning of the stress to the electrophysiology tests. ST+N2.5). 8- Rats are exposed to noise pollution for 2 hours between 8:00 AM and 12:00 PM for 12 days, and receive zinc/iron oxide nanocomposite in the amount of (25.1 mg/kg) from the beginning of the stress to the electrophysiology tests. ST+N1.25). "The single-stage sol-gel method for nanocomposites is a versatile and efficient chemical process employed to fabricate nanomaterial-based composite systems. In this method, a precursor solution (sol) containing metal or metal oxide precursors, organic or inorganic additives, and a solvent is subjected to controlled hydrolysis and condensation reactions. These reactions result in the formation of a homogeneous nanocomposite material wherein the nanoparticles (typically in the nanometer range) are uniformly dispersed within a matrix. The single-stage approach distinguishes itself by consolidating precursor preparation, nanoparticle formation, and matrix development into a single reaction step, offering advantages such as precise control over nanoparticle size and distribution, tailoring of material properties, and scalability for various applications in fields such as catalysis, electronics, optics, and energy storage."

Results: One of the ways to check the level of anxiety in different experimental groups is the plus high maze. As explained in the materials and methods chapter, it can be said that the fewer times the animals enter the open arms of the maze or the less time they spend in them, the higher their anxiety level. The analysis of the data obtained from this experiment as well as the time spent by the animal in the open arm showed that the exposure of the animals to sound stress led to anxiety behavior in them, so that the animals of the stress group had a significantly longer time than the control group. They spent less time in the open arm. On the other hand, the injection of all three doses of zinc/iron oxide nanocomposites to the animals of the

control group receiving nano caused anxiety behavior in them. Also, the injection of all three doses of zinc/iron oxide nanocomposites did not have any effect on improving the behavior of animals in the stress group receiving nano. • The results of this part of the study showed that there is no significant difference in learning and memory between the two control groups and the stress group and the control group receiving nanocomposite and the stress group receiving nano. • Disruption in learning and spatial memory is due to disruption of the HPA axis, and finally, this inefficiency can cause a decrease in granule neurons and neurogenesis in the hippocampus. • Hippocampal glucocorticoid receptors are very sensitive to increased amounts of these hormones, and high amounts of these hormones cause damage to neurons in this area of the brain. Also, in the investigation of the effect of zinc metal on learning and spatial memory, it was stated in a study that food supplements containing iron and zinc improve learning and spatial memory and also have a significant effect on motor activity. • Severe zinc deficiency in adult mice causes damage to the hippocampus and affects its function. So that memory damage was widely observed along with zinc deficiencies. • It was also shown that young and old mice with zinc deficiency have poorer spatial memory. Zinc oxide nanoparticles lead to cytotoxicity through the production of reactive oxygen species, oxidative damage, stimulation of inflammation and cell death. • Exposure to zinc vapor may have negative effects on cognition and memory, which are age- and gender-dependent. Due to the contradictory effects of nano zinc oxide in behavioral tests related to cognitive processes, memory and learning, it is difficult to identify the mechanism of their effect. Examining the data obtained from the training sessions for animals in the Morris water maze, shows that the studied animals gradually recognized the location of the hidden platform by using the spatial keys in the laboratory and also by the placement of the operator and at the same time as the number of trials increased. They spend less time to find the hidden platform and therefore travel less distance. It shows that the injection of all three doses of zinc/iron oxide nanocomposites had no effect on improving the memory of animals subjected to sound stress. Meanwhile, the injection of all three doses of zinc/iron oxide nanocomposites caused memory disorders in controlled animals. The results of graph (4-6) show that the injection of all three doses of zinc/iron oxide nanocomposites had no effect on improving the memory of animals subjected to sound stress. On the other hand, the injection of all three doses of zinc/iron oxide nanocomposites caused memory impairment in controlled animals.

Conclusion: In general, the current research shows: A) Zinc/iron oxide nanocomposites were prepared by the green method and using the modified sol-gel technique. b) Exposure of animals to sound stress caused an increase in their anxiety level. c) In the stress group receiving nano, injection of all

three doses of nanocomposite did not reduce anxiety behavior in animals. d) In the three-dose injection stress group, zinc/iron oxide nanocomposite had no effect on improving the learning process of animals. e) Sound stress caused disturbances in the spatial memory of animals, and the injection of all three doses of nanocomposite did not improve spatial memory in animals exposed to stress. f) Sound stress did not induce LTP in animals. g) Injection of nanocomposite to animals exposed to sound stress-induced LTP. Discussion and conclusion about the effectiveness of zinc/iron oxide nanocomposites prepared by the green method, there is a difference on the anxiety of rats exposed to sound stress and rats with and without exposure to sound stress. The findings of this part of the study show the destructive effect of sound stress on the anxious behavior of rats. By stimulating the hypothalamus-pituitary-adrenal (HPA) pathway, stress causes the release of cortisol hormones in humans and corticosterone in rodents, which by activating the sympathetic system increases the plasma concentration of norepinephrine hormones. Long-term exposure to sound waves leads to physiological and psychological damage that increases oxidative stress. The findings of this section are in line with most previous studies, including the studies of Ahmadi et al. (2017) and Karimi et al. (2015). suggestions According to the positive results of this research, which indicated the significant effect of zinc/iron oxide nanocomposites injection on hippocampus neuronal responses in rats, it is suggested to use this method in investigating the effects of other nanoparticles.

Keywords: Nanocomposite, zinc/iron oxide, acoustic stress, anxiety,

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The effectiveness of the teaching model of project-oriented and distance collaboration on the quality of medical education (Review)

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Introduction: The use of new and active learning and student-centered methods has been felt by the educational system and the use of these methods has been common in various sciences including medical sciences. Teaching model of project-oriented and distance collaboration (TMPODC) is an integrated method that will lead to the beneficial use of educational resources and the cultivation of talents. This study was conducted with the aim of investigating the impact of TMPODC on the quality of medical education (ME).

Methods: A systematic search of multiple bibliographic databases (Medline, EMBASE, Scopus, Web of Science, Google Scholar, PubMed and ScienceDirect), focused on using TMPODC in ME until 5th July 2023. Finally, after the data quality, we analyzed a total of 17 articles.

Results: The findings from the study of the articles showed that the educational activities in this teaching model are based on search and exploration and this has been effective in the deep learning of students. The implementation of this method had a positive effect on students' learning and collaborative abilities and has increased the empowerment of students in self-management, joint efforts, communication, self-evaluation, self-control, effective management and preparation of learning resources. This teaching model is based on modern educational theories and exercises and has empowered students in the use of software and online education. Among the important elements of this teaching model are the curriculum system, the group of instructors, the group of learners, the type of educational activities, the evaluation method and cooperative and group programs.

Conclusion: This integrated method strengthens three learning techniques including: goal-oriented active learning technique, cooperative and self-directed learning technique, and self-assessment learning technique. Therefore, this teaching model can be used as a source for modifying teaching models and improving the quality of ME in many universities.

Keywords: Teaching model of project-oriented, teaching model of distance collaboration, medical education

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The Effects of Gut Microbiota on the Nervous System (Research Paper)

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Introduction: The gut microbiota has been shown to play a crucial role in various physiological processes, including digestion, metabolism, and immune function. Recent studies have also suggested that the gut microbiota can influence the nervous system, including behavior, mood, and cognitive function. However, the mechanisms underlying these effects are not fully understood. In this study, we aimed to investigate the effects of gut microbiota on the nervous system using a mouse model.

Methods: Thirty male mice were randomly assigned to two groups: a control group and a group treated with antibiotics to deplete gut microbiota. After four weeks of treatment, the mice underwent a battery of behavioral tests, including the open field test, elevated plus maze test, and Morris water maze test. The mice were then sacrificed, and their brains were collected for histological analysis.

Results: The results showed that the depletion of gut microbiota led to significant changes in behavior, including increased anxiety-like behavior and impaired spatial learning and memory. Histological analysis also revealed alterations in the structure and function of the hippocampus, a brain region critical for learning and memory.

Conclusion: Our findings suggest that gut microbiota plays a crucial role in the regulation of the nervous system, particularly in behavior and cognitive function. Further studies are needed to elucidate the underlying mechanisms and potential therapeutic implications of these findings.

Keywords: gut microbiota, nervous system

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The effects of L-serine on histopathological changes of pancreas in diabetic mice (Research Paper)

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Introduction: Diabetes mellitus is a common metabolic disorder as a world concern. It is caused by a lack of insulin in type 1 diabetes or a combination of insulin resistance and reduced insulin production in type 2 diabetes and gestational diabetes. Thus, there is a high need for therapeutic approaches to reduce the incidence of diabetes and its related complications. Growing evidence suggests a role for L-serine in the development of diabetes mellitus and its related complications, with L-serine being positively correlated to insulin secretion and sensitivity. The aim of this study is to investigate the possible pancreas histopathological changes caused by diabetes after treatment with L-Serine.

Methods: In order to carry out this research, 18 c57bl/6 male mice were purchased and divided into 3 groups (control, diabetic control and diabetic mice treated by L-serine(. Diabetes induced by streptozotocin, (200 mg/kg). After four weeks of oral administration of L-Serine (approximately 280 mg/day/mouse), animals were euthanized and pancreas tissue was used to determine pathological changes by H&E-stained techniques.

Results: In histopathological study of pancreas in the diabetic group, we discovered atrophy of the islets of Langerhans as well as reduction in their size and number. Abnormal histological changes significantly decreased in the diabetic group that supplemented by L-Serine.

Conclusion: These findings indicate that the supplement of L-Serine may has an effective influence on diabetes-induced pancreas tissue damage. These results are a foundation to further explore the use of L-serine supplement as a novel therapeutic intervention for pancreatic disorders in diabetes mellitus.

Keywords: Diabetes, L-Serine, pancreas, histopathology

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The effects of L-serine on oxidative stress of pancreas in diabetic mice (Research Paper)

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Introduction: Diabetes mellitus is a metabolic disorder with an increasing global prevalence that can lead to premature death. High blood glucose is the main symptom of diabetes mellitus as a consequence of disorder in pancreatic insulin secretion or function. L-Serine supplementation -regarded as safe by the FDA- can improve glucose homeostasis, and can reduce homeostasis model assessment-estimated insulin resistance (HOMA-IR) and oxidative stress. The aim of this study was to investigate the effects of L-serine intake on oxidative stress indices in the pancreas of diabetic mice.

Methods: 18 c57bl/6 male mice were divided into 3 groups (control, diabetic control and diabetic mice treated by L-serine(. Diabetes induced by chemical method (streptozotocin, 200 mg/kg). After four weeks of oral administration of L-Serine (approximately 280 mg/day/mouse), animals were euthanized by guillotine and blood samples were collected to determine biochemical parameters and oxidative stress indices.

Results: The results of this study showed that the oral administration of L-Serine in diabetic mice could help to lower blood sugar level and could lead to increased catalase activity as a free radical scavenger ($p<0.05$) but had no significant effect on the level of Malondialdehyde as an end product of lipid peroxidation in oxidative stress status.

Conclusion: These findings show that the supplement of L-Serine may has an effective influence on diabetes-induced pancreas damage by lowering blood sugar and improving oxidative stress status.

Keywords: Diabetes, L-Serine, pancreas, oxidative stress

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The effects of mesenchymal stem cells-derived secretome in cancer prevention and therapy (Review)

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Introduction: Cancer is a leading death reason worldwide, and due to the growing aging population, it is a rising health problem in both developing and developed nations. By rapid advancements in therapeutic methods, using stem cells has provided novel approaches in treating cancer. The secretome term is well-defined as the collective term of the entire set of secreted proteins by cell secretory machinery since the introduction of the term by Tjalsma and coworkers in 2000. All secreted proteins either attached over the cell surface or anchored in the extracellular environment as well as the proteins consisted of the secretory pathway subtitle as the secretome.

Methods: To carry out this review, the key words mesenchymal stem cells (MSCs), Secretome, Cancer, Cell therapy from ISI, PubMed, Scopus databases and Google Scholar were searched. Based on the selection criteria, the articles that were published between 2015 and 2022 were selected and included in the study.

Results: Mesenchymal stem cells (MSCs) have shown growing promise in cancer therapy owing to their advantageous qualities. MSCs secret exosomes via paracrine signaling, which have the same impact as MSCs, as well as having the benefits of remarkable repairability, negligible immunogenicity, and targeted delivery.

Conclusion: In this review, the obtaining procedures, characteristics, biological activities, and recent discoveries regarding the influence of MSCs exosomes in cancer therapy, and a summary of inhibiting as well as promoting role of these cells on cancer progression is provided.

Keywords: Mesenchymal stem cells (MSCs), Secretome, Cancer, Cell therapy

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The Effects of Non-Alcoholic Fatty Liver Disease on Pregnancy Outcomes (Review)

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. Obesity, overweight, diabetes, smoking, hormones, and genetic were identified as risk factors for NAFLD. Pregnancy itself has a higher risk for NAFLD as well as developing insulin-resistance and hyperglycemia. The presence of NAFLD in pregnancy increases some maternal and fetal morbidities including gestational diabetes (GDM), Cesarean section, preterm labor (PTL), miscarriage, low birth weight (LBW), and Preeclampsia. This study aimed to review the association between the NAFLD and pregnancy outcomes.

Methods: This review has been conducted based on analysis of available literature indexed in PubMed database between2018 and 2022. Specific keywords including “NAFLD”, “Nonalcoholic fatty liver disease”, “pregnancy outcomes” and “gestational diabetes” have been used. Experimental and review articles on the mentioned theme were included.

Results: Accumulating evidence from studies suggests that NAFLD is a risk factor for early miscarriage, hypertension and preeclampsia. NAFLD also increases some maternal and fetal morbidities including GDM, LBW, PTL. However, a review article showed that there is not any significant association between NAFLD and C/S, LBW, and PTL. Previous studies have shown that NAFLD is also a risk factor for dysglycemia. The pathophysiology of increasing the risk of these pregnancy complications due to NAFLD is still unclear but elevating of inflammation factors because of insulin resistance can be probably one of the reasons.

Conclusion: In summary, NAFLD is associated with adverse maternal and fetal outcomes. Therefore, NAFLD should be considered a high-risk obstetric condition. Early identification of fatty liver disease is needed to minimize the implications for mother and child. It is also necessary to mention that we still need more data and studies to consider the effects of NAFLD on pregnancy outcomes.

Keywords: NAFLD, pregnancy, pregnancy outcomes, GDM.

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The effects of Zinc Oxide Nanoparticles on Taxol induced testicular toxicity in mice (Research Paper)

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Introduction: The treatment of childhood cancer with chemotherapy drugs can result in infertility in adulthood. Taxol is the brand name of Paclitaxel, is a chemotherapeutic agent able to generate reactive oxygen species (ROS) and causes male infertility. In this study, we investigated the protective role of zinc oxide nanoparticles against the destructive effects of Taxol on testicular tissue in adult male NMRI mice.

Methods: 24 adult male NMRI mice were divided into four groups: control, taxol (5mg/kg), zinc nanoparticles (5mg/kg) and taxol + zinc nanoparticles and treated for 35 days Intraperitoneally. At the end of treatment, after anesthetizing the mice, body and testis weight and tissue parameters were evaluated with stereological technique. Data were analyzed by one-way analysis of variance and Tukey test.

Results: A significant decrease was observed in the testicular weight, the volume of testicular tissue, volume, height and diameter of seminiferous tubules, spermatogenesis indices and the number of germ cells in the Taxol group compared to the control group ($p<0.001$), while the interstitial tissue volume showed a significant increase in the Taxol group compared to the control group ($p<0.05$). The simultaneous treatment of zinc oxide nanoparticles with taxol significantly reduced the mentioned parameters compared to the Taxol group.

Conclusion: These findings suggested an antioxidant potential role for Zinc oxide nanoparticles in the protection of Taxol -induced testicular toxicities.

Keywords: Taxol, Zinc Oxide Nanoparticles, Testis, Mice.

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The expression of nicotinic acetylcholine receptor subunits of skeletal muscle during myogenic differentiation of rat adipose-derived mesenchymal stem cells (Research Paper)

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Introduction: A neuromuscular junction (NMJ) is a chemical synapse between motor neurons and skeletal muscles. One of its proteins is the nicotinic acetylcholine receptor (nAChR) which is located on the membrane of skeletal muscle cells. Nicotinic acetylcholine receptors are cationic pentameric membrane proteins that are sensitive to endogenous acetylcholine (ACh). nAChRs are composed of 17 different subunits α1-α10, β1-β4, γ, δ and ε. Muscle receptors and neuroreceptors are two major groups of nAChRs. The hetero-pentameric muscle nAChRs comprise two α1 plus a β1, δ, and γ (fetal) or ε (adult) subunits. After innervation, the newly synthesized nAChR contains ε subunits instead of γ subunits. Adipose-derived stem cells (ADSCs) have been validated for their low immunogenicity and ability to self-renew, to differentiate into various tissue progenitors. Given this, adipose-derived stem cells (ADSCs) are emerging as a clinically relevant cell source for establishing human NMJs to study synaptic growth and maturation as well as disease modeling and drug discovery. This study aimed to investigate the expression of subunits of the nAChR during the myogenesis of rat ADSCs.

Methods: For this purpose, stem cells were extracted from rat fat, and myogenic differentiation was performed using 5-aza (3μg/ml) for 24 hours and

then the culture medium contained 5% horse serum. On the 3rd, 7th, 14th, 21st, and 28th days of differentiation, the Expression of subunits of nicotinic acetylcholine receptor was investigated compared to undifferentiated ADSCs (control group) using Real-time PCR and western blot.

Results: The results showed that ADSCs differentiated with 5-aza and horse serum could express nicotinic acetylcholine receptor α1, β1, δ, γ, and ε subunits ($P<0.001$). The expression of the epsilon subunit, which represents the mature subunit, is higher than the gamma subunit, which represents the embryonic subunit. In the comparison of days, the highest protein expression of the gamma subunit showed on the 28th day($P<0.0001$), and the highest amount of protein of the epsilon subunit was on the 21st day($P<0.0001$). The protein and gene expression of all subunits increased with the increase in the differentiation day.

Conclusion: The findings can be used in the study of skeletal muscle evolution. Additionally, data may be employed to develop innovative procedures to treat skeletal muscle disorders.

Keywords: nicotinic acetylcholine receptor, nAChRs , neuromuscular junction, NMJ, rat adipose-derived stem cel

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The fucoidan content within three dominant species of brown macroalgae from Persian Gulf: presenting a bioactive candidate compound for functional food development (Research Paper)

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1.
2.

Introduction: Fucoidan is a multipart bioactive sulfated fucan dispersed in numerous marine organisms, and the Phaeophyceae (brown seaweeds) are reported as the major producer. It is a water-soluble heteropolysaccharide which the exact constructional features have not yet been clarified. Fucoidan is comprised of fucose, uronic acids, galactose, xylose and sulphated fucose. The worth of brown algal fucoidan is favored to fucose-comprising glycans owing to its diverse branches and molecular weights, which enhances its demands as functional ingredient in food, health products, and pharmaceutics. Fucoidan extracted from brown seaweed have numerous major physiological roles comprising anticoagulant, anticancer, anti-inflammatory immunostimulatory, antioxidant, neuro/cardio protection and growth-promoting function. In addition, fucoidan can postpone the Transfusion Reaction Symptoms, hepatic disorders, osteoarthritis, and kidney disease, reduce the risk of radiation destruction, and can even constrain some snake venom.

Methods: Sargassun muticun , Sargassum ilicifolium , Padina sp were collected from coastal waters around Bushehr, Persian Gulf. These algae were cleansed using tap water, preserved by exposure to the sun, and then desiccated in a 60°C oven. Finally, they were powdered and stored in a 4°C ice box until further analysis. Fucoidan were extracted by acid treatments at 70–100 ◦C overnight. The fucoidan subsequently was separated from alginate, by precipitation of alginate with CaCl2. Then the supernatant was gathered and combined with 100% ethanol and stored for precipitation. The precipitate was dissolved in sterile deionized water using a membrane filter and incubated for two days at 4 °C. Later, the solution was freeze-dried.

Results: The fucoidan content extracted was 18.5 % (of dry weight), 18.62 %, and 22.44 % from Sargassum muticum, Sargassum ilicifolium and Padina sp, respectively.

Conclusion: The current investigation found that purifying algal ingredients with CaCl2 can improve fucoidan yields. The present study also exhibited that

Sargassum ilicifolium and Padina sp were the ideal sources for extracting fucoidan. According to the results, the obtained fucoidan proportions were higher than those reported formerly which used multistep extraction in S. horneri and L. japonica, yielding 6.90% and 6.34% fucoidan, respectively. Alternatively, gained proportions were comparable with those reported for Sargassum glaucescens, Sargassum horneri, and Laminaria japonica, yielding 13.13%, 24.00%, and 22.67% from respectively. Since, the biomass of the Sargassum ilicifolium and Padina sp is much larger in the Persian Gulf, we consider Sargassum ilicifolium and specially Padina sp to be rich sources of fucoidan for human consumption.

Keywords: Fucoidan, Brown Macroalgae, Extraction, Yield, Persian Gulf.

The function and importance of Crisper technique in the treatment of Brest cancer (Review)

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Introduction: Advances in the treatment of breast cancers (BCs) have led to significant improvements in the overall survival of patients. Local therapies, including surgery and radiotherapy, in conjunction with adjuvant targeted therapies and chemotherapy are the mainstays of BC treatment. in contrast to earlier genome editing systems, which mediate sequence recognition through protein-DNA interactions, the CRISPR/Cas system uses an RNA molecule to mediate binding. It is derived from a prokaryotic adaptive immune system protecting against invading viruses and plasmids and is composed of CRISPR loci, comprised of alternating repeat-spacer units, and CRISPR-associated (Cas) proteins. Immunisation occurs in three stages: (i) adaptation, in which invading nucleic acids are cleaved by a complex of Cas endonucleases and the resulting fragments, called protospacers, are integrated into CRISPR loci between identical repeats; (ii) expression, in which the locus is transcribed into pre-CRISPR RNA (pre-crRNA) and processed into individual CRISPR RNA (crRNA) molecules; and (iii) interference, where the crRNA directs a single Cas endonuclease or a protein complex to cleave the foreign nucleic acids. The aim of this study was to evaluate the function and importance of the Crisper technique in the treatment of breast cancer.

Methods: This is a review that was conducted by searching PubMed, Google Scholar, and Google with the subject of the function and importance of the Crisper technique in the treatment of Brest cancer

Results: The result showed Genome editing system is based on the use of engineered nucleases composed of sequence-specific DNA-binding domains fused to a non-specific DNA cleavage module These chimeric nucleases induce DNA double-strand breaks (DSBs) that stimulate the cellular DNA mechanisms, including error-prone non-homologous end joining (NHEJ) and homologous recombination (HR) Several approaches have been used in the last years as genome editing technologies. Breast cancer (BC) is the most common type of cancer in women at the global level and the highest mortality rate has been observed with triple-negative breast cancer (TNBC). Accumulation of genetic lesions aberrant gene expression and protein degradation are considered to underlie the onset of tumorigenesis and metastasis. Therefore, the challenge to identify the genes and molecules that

could be potentially used as potent biomarkers for personalized medicine against TNBC with minimal or no associated side effects. Discovery of the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR associated protein 9 (Cas9) arrangement and an increasing repertoire of its new variants has provided a much-needed fillip towards editing TNBC genomes.

Conclusion: the recent availability of genome-editing tools such as CRISPR-Cas9 is an important means of advancing functional studies of breast cancer through the incorporation, elimination, and modification of somatic mutations and fusion genes in cell lines and mouse models. These tools not only broaden the understanding of the involvement of various genetic alterations in the pathogenesis of the disease but also identify new therapeutic targets for future clinical trials.

Keywords: Brest cancer, CRISPR-Cas9, Genome editing

The Function of LncRNA H19 in Ovarian Cancer: A Potential Biomarker for Early Diagnosis (Review)

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Introduction: Ovarian cancer (OC) is the most lethal gynecologic cancer worldwide, The morbidity of OC is ranked the eighth among the most common women malignancies. Due to a lack of reliable biomarkers at the early stage, most ovarian cancer cases are diagnosed at advanced stages (stage III or IV), with extensive peritoneal metastasis, making the 5-year survival rate as low as 30%. Hence for better management (prediction, progression, and response to treatment) of ovarian cancer, there is a need for new biomarkers. Long non-coding RNAs (lncRNAs) are a class of RNA with over 200 nucleotides with no protein-coding capacity. LncRNAs participate in many physiological and pathological processes, including apoptosis, cell proliferation, invasion, and carcinogenesis. Numerous reports of dysregulated lncRNA expression across different cancer types including ovarian cancer suggest that abnormal lncRNA expression may significantly contribute to tumorigenesis. The aberrant expression of lncRNAs in ovarian cancer could mark the spectrum of disease progression. LncRNAs often have tissue-specific patterns that differentiate them from miRNAs and protein-coding mRNAs, which are expressed in a variety of tissues. Some lncRNAs may be isolated non-invasively from blood and have high stability while circulating in body fluids. These characteristics make them suitable for cancer diagnostic and prognostic biomarkers especially when included in exosomes or apoptotic bodies.

Methods: For the literature review, we searched Scholar, Web of Sciences, PubMed/MEDLINE, and Scopus databases, and articles published until 2023 were included. The keywords and terms of the major concepts for this review were ovarian cancer, long non-coding RNA, ovarian cancer diagnosis and prognosis, ovarian cancer biomarkers, and H19, which were developed and combined to form the search strategy.

Results: LncRNA H19 (H19) was one of the first discovered lncRNAs and is encoded by the H19 gene. H19 is associated with malignancies detected in the early stages. Studies have shown that H19 plays an important role in the

proliferation, invasion, and migration of OC. H19 could act as an oncogene in ovarian cancer cells, and via sponging miR-675. A study on the chemoresistant A2780 cell line revealed that H19-derived miR-675 participates in the progression of ovarian cancer by up-regulating of transcription factor slug which results in the down-regulation of the E-cadherin as an epithelial marker. In a study conducted by Medrzycki et al., H19 was an oncogene that is synergistic with histone H1.3 inhibiting the proliferation of OC cells. Yan et al. showed that Let-7 was a tumor suppressor, and the overexpression of H19 reduced the bioavailability of Let-7, contributing to the occurrence and development of cancer to a certain extent. Sajadpoor et al. found that valproic acid could reduce the expression of H19 in OC tissues, thus inhibiting cell proliferation. Therefore, H19 may play a key role in the early diagnosis of OC and may be a novel therapeutic target.

Conclusion: In this narrative review, we shed light on the molecular mechanism of H19 in OC development and pathogenesis. Moreover, we discussed the expression pattern and importance of H19 as a potential biomarker in early OC diagnosis.

Keywords: RNA, Long Noncoding; Ovarian Neoplasms; H19 long non-coding RNA; Biomarkers

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The future of cancer treatment: advancing immuno-radiotherapy with innovative techniques (Review)

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Introduction: For the majority of cancer types, radiotherapy has been used to treat them since the early 1950s, and it is one of the most widely used treatments today. The induction of tumor cell death by ionizing radiation has the effect of either eliciting Immunosuppression or immune responses that protect against tumors, which contributes to the recurrence of local tumors after radiation treatment. There is a growing body of evidence that immunosuppression has the potential to lead to the Activation of immune suppressor cells, such as neutrophils, tumor-associated macrophages (TAMs), T regulatory cells (Tregs), myeloid-derived suppressor cells (MDSCs), as well as the release of immunosuppressive cytokines (TGF- β, IL-10) and chemokines. As a combination with RT, it has been shown that many primary and metastatic cancers can be treated with immunotherapies based on checkpoint blockade. . These immunotherapies include anti-PD-1 and anti-PD-L1 antibodies. It is also known that RT can be enhanced by using vaccines, cytokines, immunoglobulins, and adaptive immune cells transferred from one patient to another (NK cells, T cells, DCs). In the present review, we will summarize the currently available data on the immunological rationale behind the combination of RT with various immunotherapies.

Methods: In order to retrieve published data (from 2000 to 2023), databases including Scopus, PubMed, ScienceDirect, and Google Scholar were used. This search strategy involved downloading and retrieving published literature. There were specific keywords used in the search, such as " radiotherapy ", ”immunotherapy”, ”immune suppressor cells”, ” immunosuppressive cytokines”, ” immunosuppressive chemokines”. In total, 500 studies have been conducted. A total of 400 abstracts were excluded, and 100 full-text studies were read. An analysis of 30 relevant articles with complete abstracts was conducted in the final inclusion criteria.

Results: One of the novel approaches for improving the effectiveness of immuno-radiotherapy is the integration of cutting-edge immunotherapies with radiation therapy to enhance the immune system's response to cancer and enhance the immune system's ability to fight cancer. A customized treatment plan is developed for each patient based on their immune profile and tumor characteristics, and immune checkpoint inhibitors and adoptive cell therapies are combined with radiation therapy for treatment. Researching the development of innovative immunomodulatory substances like STING agonists and oncolytic viruses for reducing immune suppression. In addition, we are fine-tuning radiation doses to reduce immune suppression and experimenting with specialized immunomodulatory substances, such as nanoparticles, for precise radiation delivery and immune regulation. As a result of the synergy between radiation and immunotherapy, cancer patients with these innovative approaches will have better long-term survival outcomes and better control of their tumors. Researchers have shown that patients with advanced non-small cell lung cancer have a significant improvement in local control of metastatic tumors and improved overall survival when they combine immune checkpoint inhibitors (such as pembrolizumab or nivolumab) with stereotactic body radiation therapy (SBRT). The researchers have successfully engineered nanoparticles coated with immune-stimulating agents, such as toll-like receptor agonists, and these nanoparticles are demonstrated to have remarkable tumor-targeting capabilities when combined with radiation therapy in preclinical models. It has been shown that oncolytic viruses can be used together with radiotherapy to promote tumor-specific immune activation in a way that has proven to be very effective. A cancer cell is selectively infected and destroyed, and immune cells are recruited to mount a powerful antitumor response, increasing the chances of a successful therapeutic response.

Conclusion: In view of these developments, immuno-radiotherapy holds great promise as a cancer treatment and could be used in the future. A number of new approaches are currently being explored and developed to enhance its efficacy in order to make it more effective. As research and clinical teams strive to maximize the therapeutic potential of radiation therapy and immunotherapy, a combination of personalized treatment plans, immunomodulatory agents, and innovative delivery systems is being explored. The purpose of these efforts is not only to expand our understanding of the complex interactions between radiation and the immune system but also to improve patient outcomes, minimize treatment-related toxicity, and push the boundaries of cancer treatment in the process. Continually developing these novel strategies holds substantial promise for the future development of cancer therapies and the possibility of providing renewed hope to those who suffer from the disease.

Keywords: radiotherapy,immunotherapy,immune suppressor cells,immunosuppressive cytokines

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The gut immune system effect on cardiovascular disease (Review)

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Introduction: Increased risk of cardiovascular disease (CVD) is associated with significant changes in the human gut microbiota, particularly in conditions such as coronary atherosclerotic heart disease, hypertension, and heart failure. Immune mechanisms are important to maintain the dynamic balance between the gut microbiota and the host. to the immune system, when that balance is disturbed by either of these changes in the host, it can cause varying degrees of damage to the host, leading to progressive disease progression over time. This review provides insight into the immune mechanisms associated with the gut microbiota and its metabolites in general cardiovascular disease. It explores how dysfunction of the gut-cardiac axis contributes to CVD progression and describes current effective approaches to modulate the gut microbiota as a potential treatment strategy for CVD.

Methods: Five databases were comprehensively searched to identify articles published between January 2002 and January 2023 on the role of the gut immune system in cardiovascular disease. A total of 500 studies were funded using the keywords cardiovascular disease, immune system, gut immunity, and gut immunity. 100 went to read the whole text. The search included 25 relevant articles with full abstracts.

Results: The role of the gut microbiota is closely related to the likelihood of cardiovascular disease. The development of cardiovascular diseases due to physiological disturbances of the intestinal microflora involves three main processes: deterioration of the integrity of the mucosal barrier, excessive inflammation, and dysfunction of the immune system. Structural components present in Gram-negative bacteria, especially LPS, maybe the main cause of intracellular toxicity and impairment of intestinal mucosal barrier function. LPS may be associated with the occurrence of cardiometabolic disorders. Additionally, studies have shown that a high-fat diet can reduce the number of gram-positive bifidobacteria in the gastrointestinal tract and increase the number of LPS-containing gut bacteria, both of which contribute to obesity. , which is a major risk factor for cardiovascular disease. Importantly, long-term subcutaneous LPS infusion altered their glucose metabolism and weight gain

in a manner similar to that of a high-fat diet. Consequently, intestinal dysbiosis and related changes in metabolic products lead to insulin resistance, increased adipose tissue deposition, and abnormal nutrient metabolism, increasing the likelihood of developing cardiovascular risk factors such as obesity and diabetes.

Conclusion: The relationship between cardiovascular disease and gut microbiota and their metabolites has gradually gained recognition, with several distinct features associated with gut microbiota composition and metabolite profiles that are closely intertwined with the host's innate and adaptive immune system, mostly through interactions with bacterial components. . and metabolites are initially the first line of defense as physical barriers, while immune cells such as macrophages, dendritic cells and neutrophils bind to the gut microbiota and its metabolites. These interactions may have deleterious effects that may accelerate the progression of the microbial gut-heart axis concept in cardiovascular disease. explain the relationship between gut microbiota and cardiovascular disease, emphasizing the role of dysbiosis and bacterial translocation theories, resulting in therapies such as dietary modification, antibiotics, probiotics and transplantation of faecal microbiota from healthy donors currently being used or considered. used in clinical settings to relieve clinical symptoms. and prevent the progression of cardiovascular disease, but further investigation into the complex mechanisms underlying cardiovascular disease caused by certain metabolites (eg, trimethylamine oxide tmao) is warranted. In addition, the interaction between intestinal microorganisms and metabolic products of the host immune system is a promising new tool for prevention and metabolism. Treatment of Cardiovascular Diseases The main goal of investigating the immune mechanisms linking CVD and the gut microbiota and its metabolites is to provide potential guidance for the development of versatile and effective cardiovascular therapies.

Keywords: Cardiovascular, Immunology, Health

The healing effects of platelet rich plasma and exosomes derived from stem cells on the spermatogenic proteins and sperm parameters of non-obstructive azoospermia model rats (Research Paper)

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Introduction: Azoospermia with two types of obstructive (OA) and non-obstructive (NOA) accounts for a significant percentage of male infertility. Patients with NOA are unable to have children of their own, and they usually have to resort to adoption or the use of donated sperm. Due to the irreversible nature of spermatogenesis damage in patients with NOA, testicular biopsy and assisted reproductive techniques are the only ways to obtain biological offspring. However, these methods have limited success and do not work for all cases. Therefore, the current challenge is to improve the spermatogenic function of azoospermic men to generate sperm in their ejaculate or to improve the probability of successful sperm retrieval from the testis for ICSI. In this way, researchers are recently trying to develop treatments based on stem cell transplantation for azoospermia. It has been shown that extracellular vesicles (EVs) derived from mesenchymal stem cells (MSCs) are the main agents responsible for exerting the paracrine effects and consequently biological functions of MSCs, which offer significant advantages in the field of regenerative medicine compared to their cells of origin. EVs can bypass most of the safety considerations associated with direct cell transplantation, and unlike transplanted cells that cannot be recovered, treatment using EVs is not permanent and can be easily stopped if adverse effects occur. An autologous concentration of human platelets in a small amount of plasma is known as platelet-rich plasma (PRP). The generation of reproductive hormones and improvement of spermatogenesis in patients with poor sperm parameters, as

well as testicular torsion are both enhanced by the platelet-rich plasma. In this study, comparative effect of exosomes obtained from MSCs derived from adipose tissue (AD-Exo) and PRP was evaluated on the recovery of spermatogenesis in non-obstructive azoospermia model rats.

Methods: We examined the effects of human PRP and exosomes generated by adipose tissue-derived MSCs (AD-MSCs) on the restoration of spermatogenesis after intra-testis injection in NOA rat models, which was carried out on 30 male 8–12 weeks old Wistar rats classified in 5 groups. AD-MSCs were obtained and grown up to passage 3 in the cell culture facility. The exosomes were then isolated from conditioned medium of the cells. In addition, we collected peripheral blood from willing donors and PRP was separated. Rats were given two intraperitoneal injections of busulfan (10 mg/kg body weight) with 21 days interval in order to generate NOA model. Intratesticular injection of 100 microliters of exosomes (500 mg/mL), 100 microliters of PRP, and 100 microliters of PBS was done in the AD-Exo, PRP, and sham groups, respectively, at the time points of three days and two weeks after induction. The NOA-induced rats with no treatment were considered as the positive-control (NOA) group and the healthy rats with no induction and no treatment were supposed as negative-control group. Two months after final medication, the rats were put down for further research. In order to investigate the changes in different groups of NOA model rats, western blot analysis was done for DDX4 and DAZL protein. In addition, the amount of count and motility in the rat sperm samples of different groups were evaluated. Finally, the resulting data were statistically analyzed using SPSS software.

Results: Based on the analysis of the experimental groups, it was discovered that the expression of the DAZL and DDX4 was significantly higher in the AD-Exo and PRP treatment groups than in the control group, while it was significantly decreased in the NOA and sham groups ($p \leq 0.05$). The DAZL and DDX4 protein appears to be restored as a result of exosome and PRP treatment. In addition, compared to the control group, sperm parameters were considerably greater in the AD-Exo and PRP treatment groups, while they were substantially reduced in the NOA and sham groups ($p \leq 0.05$).

Conclusion: This investigation verified the beneficial effects of PRP and exosomes released by AD-MSCs on the spermatogenesis-related proteins and sperm parameters. To ascertain the therapeutic benefit of these medications on patients with NOA, it is evident that more research on testicular histology, size and weight of testis is needed.

Keywords: Spermatogenesis, Sperm parameters, Non-Obstructive Azoospermia, Platelet Rich Plasma, Exosome, MSCs

The Impact of Artificial Intelligence on the Healthcare Workforce: Implications and Challenges (Review)

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Introduction: The remarkable advancement of artificial intelligence (AI) technologies, particularly within the healthcare sector, is indisputable. This review critically examines the profound implications of AI on the health human resource (HHR) landscape. The primary objective is to comprehensively analyze how AI integration influences various dimensions of the healthcare workforce.

Methods: To identify relevant literature, a search strategy was employed, combining keywords like "artificial intelligence," "healthcare workforce," and "AI". Databases including PubMed, Google Scholar, and Embase were rigorously searched until June 2023. The inclusion criteria were journal articles written in English, providing full-text access, and exclusively investigating AI's effects on the healthcare workforce, while studies beyond the healthcare domain were excluded.

Results: AI's applications in healthcare encompass a broad spectrum, ranging from clinical decision support and administrative task automation to automated imaging, drug design, and surgical robotics. Consequently, AI engenders multifaceted impacts on the HHR. The outcomes of AI implementation can be categorized as follows: Performance enhancement, productivity amplification, workload mitigation, workflow optimization, satisfaction improvement, and transformation of physician-patient relationships. AI-driven technologies adeptly tackle labor and time-consuming tasks, resulting in providing more free time for healthcare professionals to do more complicated tasks. Radiologists, for instance, benefit from expedited scan interpretation and more precise diagnoses, alleviating their workload. The integration of AI also revolutionizes healthcare workflow through advancements in clinical documentation, quality-measurement reporting, and point-of-care learning. These innovations automate mundane tasks, allowing physicians to focus on tasks that demand human expertise, fostering satisfaction among both healthcare providers and patients. Notably, patient safety is improved by AI. However, the leveraging of AI in healthcare has its own challenges. Addressing regulatory, legal, and ethical concerns surrounding AI implementation is imperative. Privacy concerns, scarcity of

infrastructure, data availability, and economic considerations pose critical challenges. The economic aspects of AI integration encompass both upfront investment costs and potential long-term financial benefits through increased efficiency and improved patient outcomes. It is to be noted that although AI offers higher productivity, improved productivity and increased return on investment, it cannot replace all human labor.

Conclusion: In conclusion, the integration of AI into healthcare is transformative and pervasive. AI acts as a valuable aide in the healthcare domain, augmenting efficiency and healthcare quality, , while its economic implications need to be carefully evaluated. However, the envisioned scenario of complete human workforce replacement remains implausible. Embracing the benefits of AI necessitates a holistic approach that addresses multifarious challenges spanning legal, ethical, and economic dimensions.

Keywords: Artificial Intelligence, Healthcare workforce, AI integration

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The Impact of Ozone Layer Depletion and Global Warming on Skin Cancer Prevalence in Iran (Review)

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Introduction: The ozone layer, a natural shield, effectively absorbs the majority of the sun's ultraviolet radiation. However, with the advent of industrialization in various nations towards the end of the 20th century, the degradation of this protective layer has commenced, leading to an escalation in the proportion of UV-B rays reaching the Earth's surface. A recent study has further revealed that a long-term temperature increase of two degrees Celsius, a consequence of global warming and climate change, amplifies the carcinogenic effects of solar UV by 10%. Prolonged exposure to sunlight has been implicated in the incidence of other skin cancers such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and other skin malignancies. This research paper delves into the factors contributing to the prevalence of melanoma in Iran and explores commonly employed treatment strategies.

Methods: The essay focuses on melanoma, providing information about its origin, subtypes, and statistics; furthermore, it presents information in a clear and organized manner, using citations to support its claims.

Results: 1. There is a significant correlation between prolonged and frequent exposure to UV rays and the prevalence of skin cancers, especially in areas of the body that are often exposed to sunlight such as the face, neck, and hands. 2. The increase in melanoma cases in Iran can be attributed to various climatic and non-climatic factors. These include the depletion of the ozone layer, global warming, and increased exposure to sunlight due to outdoor activities. 3. The high costs associated with cancer treatment in Iran, coupled with limitations in selecting effective treatment methods for melanoma, highlight the urgent need for increased public awareness about the necessary precautions against harmful sun rays. 4. Enhancing public knowledge about the potential consequences of long-term exposure to ultraviolet rays is crucial and should not be overlooked.

Conclusion: Skin cancers, particularly prevalent in sun-exposed areas like the face, neck, and hands, highlight the link between UV exposure and skin cancer. Melanoma cases in Iran have increased due to factors like ozone

layer depletion, global warming, and outdoor activities increasing sunlight exposure. The high costs and limitations of cancer treatment in Iran necessitate public awareness campaigns about sun protection. Additionally, educating the public about the risks of long-term UV exposure is crucial.

Keywords: Skin cancers, Sun-exposed areas, UV exposure, Melanoma

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The importance of human bodifluids in proteomic biomarker detection in multiple sclerosis RRMS patients. (Review)

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Introduction: Multiple sclerosis is a chronic inflammatory-autoimmune disease in the central nervous system, which is associated with inflammatory demyelination in the focal areas of axons. Among the different phenotypes of patients with MS, the relapsing-remitting MS phenotype is known as the most common phenotype in MS patients, which is associated with blood-brain barrier disorder and inflammation and recurrence of nerve attacks in the phase (Relapse) is compared to the improvement phase of attacks (Remission). For this reason, the two phases of Relapse and Remission show a very different course and progress compared to each other. Despite advances in MS diagnostic criteria such as Magnetic Resonance Imaging (MRI) and the evaluation of immunoglobulin G (IgG) in cerebrospinal fluid (CSF), which are known as the gold standards in the diagnosis of MS, the low specificity of MRI and other tests.

Methods: We selected the characteristic proteomics and multiple sclerosis keywords from Mesh in NCBI. Then we searched proteomics and multiple sclerosis in Scopus and PubMed databases to publish a specific subject about the importance of human body fluids and MS. In the following, the gained and related articles are summarized and discussed.

Results: Diagnostic problems in the diagnosis, prediction of progression, and relapse of MS disease, and the heterogeneous and unpredictable course and progression of RRMS etiopathology have faced a severe challenge in the diagnosis and prognosis of recurrence of neurological attacks in this disease.

Conclusion: This doubles the identification of efficient biomarkers involved in the pathogenesis of neurological attacks with high specificity and sensitivity by proteomic analysis of clinical samples in RRMS patients.

Keywords: Proteomics, Multiple Sclerosis, RRMS

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The Importance of Nanomedicine in Hepatocellular Carcinoma (Review)

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Introduction: The most frequent type of primary liver cancer (HCC) is also the fifth most common cancer worldwide. It has a high mortality rate and kills more than 600,000 people per year. The majority of HCC patients are detected at advanced stages of the disease, when there are few and inefficient therapy choices available because of the insidious growing characteristic of the disease. Nanotechnology has emerged as a rapidly developing topic and a cutting-edge way to address the difficulties currently facing HCC therapy. Investigating Nanomedicine in Hepatocellular Carcinoma was the goal of this investigation.

Methods: This review study has written the from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Recent research has highlighted the link between tumor cells and their surrounding microenvironment along with the fundamental role of the tumor microenvironment in hepatocarcinogenesis The tumor microenvironment is composed of; cells such as hepatic stellate cells, fibroblasts, immune cells, including regulatory and cytotoxic T cells and tumor-associated macrophages (TAMs), and endothelial cells, proteolytic enzymes including matrix metalloproteinases (MMPs) and tissue inhibitor of metalloproteinases (TIMPs), growth factors, for example, transforming growth factor b1 (TGF-β1) and platelet-derived growth factor (PDGF), inflammatory cytokines, and extracellular matrix (ECM). The EPR effect increases nanoparticle accumulation at the tumor site resulting in a more specific therapeutic targeting along with reduced toxicity of the therapeutic agents due to membrane hyperpermeability and absence of basement membrane in the tumor vasculature compared to normal tissue blood vessels pharmaceutics. Although the liver vasculature inherently possesses leaky vessels, the vasculature abnormalities in the presence of chronic liver diseases such as cirrhosis are ubiquitous Therefore, designing and developing different nano systems with particle size within the vasculature to selectively target HCC tumor cells would enable an effective drug delivery system in the setting of liver diseases. Another characteristic of the HCC tumor environment is the low extracellular pH, which lies between 6.0 and 7.0 as compared to normal tissues and blood with pH. This is due to the increased rate of glycolysis

leading to the accumulation of lactic acid in hypoxic tumor cells. Changes in pH play a role in the delivery of therapeutic agents to the liver tumor cells: an acidic pH favors the cellular uptake of weakly acidic drugs and delays the uptake of weakly basic drugs. This consideration can also inform the synthesis of nanoparticles to provide optimal HCC tumor targeting.

Conclusion: The cutting-edge research and development in HCC nanomedicine have provided a powerful tool over traditional approaches for specific tumor targeting. Although designing a nano-drug delivery system is a complex process that requires optimization of its physicochemical properties, targeting HCC cells also requires a thorough understanding of the challenges such as a cirrhotic liver setting and the interaction between nanoparticles and the HCC tumor environment hindering its transition to clinical practice. There are several significant advantages of nanotechnology, ranging from effective targeting to reduced systemic toxicity. Currently, the only FDA-approved nanomedicine for various other cancer treatments includes; Doxil (liposomal doxorubicin), Onivyde (liposomal irinotecan), Abraxane (albumin-particle bound paclitaxel), Eligard (leuprolide acetate), and Vyxeos (liposomal cytarabine and daunorubicin) with none specific to HCC. Interestingly, the most crucial part of designing HCC nanomedicine requires formulating nano systems with ligands specific to the receptors discussed above, such as ASGPR, GPC3, TfR, FR, and SR-B1. Nano systems with such targeting ligands have proven their efficacy for anti-cancer treatment in several in vitro and in vivo studies. Therefore, there has been progressive development in specific targeted nano delivery systems for HCC, and there is excellent potential for translation of this strategy into the clinical context.

Keywords: Nanomedicine, Hepatocellular Carcinoma, tumor targeting

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The Influence of Genes Involved in Obesity (Review)

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Introduction: The high prevalence of obesity and its associated diseases is a major problem worldwide. Genetic predisposition and the influence of environmental factors contribute to the development of Obesity. Obesity is a complex multifactorial abnormality that has a well-confirmed genetic basisHowever, the problem still lies in identifying the genes linked to body mass and composition. There fore, ,this study aimed to analyze associations between genes FTO,FABP2,LEPR,MC4R and LEP.

Methods: In this review, variants in genes associated with adipocyte function are examined but variants are in genes associated with metabolic aberrations and the accompanying disorders in visceral Obesity Overexpression of FTO in the diet with the positive regulation of lipogenic genes causes an increase in triglycerides and the prevalence of metabolic syndrome is strongly related to Obesity.

Results: Therefore it is associated with high food consumption, especially a high-calorie, high-carbohydrate diet, as well as the expression of genes involved in lipolysis

Conclusion: Based on This Genes, Each Person’s Diet& Life Style Can be Determined.

Keywords: Gene,Obesity,FABP2

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The LDLR rs2228671 CC genotype is associated with lower BMI in men with diabetes mellitus (Research Paper)

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Introduction: Type 2 Diabetes Mellitus (T2DM) is a chronic and age–related inflammatory disease. Although cardiovascular complications in patients with DM are common, the exact relation between DM and Cardiovascular Diseases is still unknown. LDL receptor (LDLR) is responsible for regulating plasma LDL-cholesterol concentrations and can associate with Insulin receptor on the cell membrane. This binding decreases the LDL particle clearance and can be modulated by the insulin level. Among LDLR polymorphisms, rs2228671 single nucleotide polymorphism (SNP) (C>T) has shown the strongest association with LDL-cholesterol level. In this study we evaluated the genetic link between LDLR and progression of atherosclerosis in diabetic and non-diabetic individuals.

Methods: Our study was conducted on 485 individuals who resided in Fars province of Iran. Based on the Diagnostic Angiography, patients were categorized to diabetes+angio+ (n=63), diabetes+angio- (n=48), and diabetes-angio+ (n=118) groups. Also 256 healthy blood donors were recruited and considered as control group (diabetes-angio-). DNA was extracted from peripheral blood by salting out method and LDLR gene polymorphism was detected by RFLP- PCR.

Results: We did not observe any significant difference in LDLR rs2228671 genotypes and alleles between the four groups. However, comparison of the 3 patients' groups by regression analysis showed that CC genotype was increased significantly in men who had BMI lower than 25 (P=0.043). Accordingly, the frequencies of men and women with BMI<25 and CC genotype were 80% and 20%, respectively. While the frequencies of men and women with BMI>25 and CC genotype were 57.6% and 42.4%, respectively.

There was also a significant difference between the 3 patients groups based on smoking status (P=0.005), gender (P=0.003) and blood pressure (P=0.001). Only 10.3% of smokers were diabetes+angio+, but 79.5% of smokers were diabetes-angio+. While 47.8% of female patients were diabetes+angio+, 67.9% of male patients were diabetes-angio+. Of those patients who had hypertension 45.9% were diabetes+angio+ while 76.8% of those without hypertension were diabetes-angio+.

Conclusion: We suggest that genetic variations in LDL clearance pathways may affect the progression of atherosclerosis in diabetic patients. The association of CC genotype with lower BMI may also have a protective role against diabetes in men. Also, hypertension plays a more significant role than smoking in progression of atherosclerosis in diabetic patients.

Keywords: LDLR, Diabetes Mellitus, Angiography, hypertension

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The link between diabetes mellitus type 2 and hepatocellular carcinoma; metformin treatment review article (Review)

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Introduction: The term “HepatoCellular carcinoma (HCC)” has come to be used to refer to primary liver cancer that appears from a mutation of a cellular gene and causes the cells to reproduce in a disorderly and unusual way. Also, it is recognized as being the sixth most common cancer worldwide responsible for the diagnosis of more than half a million people around the globe every year. For many years Type 2 diabetes mellitus (T2MD) has been considered an independent risk factor for HCC and interestingly the correlation is related to non-alcoholic fatty liver disease (NAFLD); a major cause of liver-related mortality. An increasing number of studies have found that obesity and insulin resistance are the strongest indicators that exist between T2DM and NAFLD. This theorem states that adipose tissue in obese people goes through changes that cause the release of a hormone called adipokine. In the condition of obesity, adipose tissue produces a higher amount of adipokine which causes insulin resistance (IR) in most cases. Insulin resistance is a common trait in NAFLD patients and it is evaluated as the major contributor to the development and advancement of the disease.

Methods: Insulin resistance is a common trait in NAFLD patients and it is evaluated as the major contributor to the development and advancement of the disease. Insulin resistance and compensatory hyperinsulinemia cause elevated manufacturing of insulin-like growth factor1, which in addition promotes hepatic cellular proliferation and inhibits cellular apoptosis in the liver. Further analysis shows that IR is affected in the progression of hepatic steatosis and hepatic fibrosis by the existence of increased circulating levels of free fatty acids which stimulate NAFLD. As mentioned previously unnatural glucose and lipid metabolism, hyperinsulinemia, and insulin resistance cause intrahepatic fat assemblage which boosts the development of HCC.

Results: More recent evidence reveals that the metformin may have direct and indirect mechanisms. The direct mechanism developed by metformin is the reduction of plasma insulin levels. On the other hand, the inhibition of carcinogenesis, the induction of cellular apoptosis, and the stimulation of the immune system are posed as indirect mechanisms of metformin.

Conclusion: Many attempts have been made to improve insulin sensitivity and reduce its resistance as well as hyperinsulinemia. There is a considerable amount of literature on the association between the use of metformin and a lower risk of HCC while the use of insulin has been related to a higher risk of HCC. Metformin is identified as a drug that functions as an endothelial protector that hampers tumor growth, and metastasis via a signaling network. Compared with exogenous insulin which increases plasma insulin levels and promotes body weight gain, metformin reduces body weight and hyperinsulinemia, improves hepatic insulin resistance, decreases steatosis, and improves liver enzymes. Metformin treatment has been independently associated with decreasing the proceeding of HCC and liver-related deaths.

Keywords: Hepatocellular carcinoma, Diabete mellitus type 2,Insulin, NAFLD, Metformin

The Mechanism of Acrylamide-Induced Neurotoxicity (Review)

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Introduction: Acrylamide is responsible for developmental genotoxicity, neurotoxicity, and potentially carcinogenicity, of which neurotoxicity has been confirmed via human and animal experiments. Therefore, neurotoxicity is closely connected with human health. For decades, results showed similar phenotypical neurotoxicity in various laboratory animals, including dogs, cats, guinea pigs, rabbits, and rodents when repeatedly exposed to ACR levels ranging between 0.5 and 50 mg/kg/day. These neurological disorders may be caused by covalent adduct formation between highly nucleophilic cysteine and ACR at the active location of the presynaptic neuron. This process deactivates neurons and impacts neurotransmitter transfer, leading to neurotoxicity. Moreover, oxidative stress serves as a biochemical and physiological activation signal and is, directly and indirectly, related to the neurotoxicity caused by ACR. Although the potential molecular mechanism reported in recent years as underlying ACR-related neurotoxicity is multifaceted, a complete characterization and summary of the comprehensive mechanical system and its impact are still required. The aim of this study was to investigate The Mechanism of Acrylamide-Induced Neurotoxicity.

Methods: This review study has been written by The Mechanism of Acrylamide-Induced Neurotoxicity from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Acrylamide is a small-molecule hydrophilic substance. It is absorbed via the gastrointestinal tracts of humans and animals and passively diffused to the entire body. ACR can also pass through the blood-brain barrier to directly exert its toxic effect on the nervous system. ACR follows two main metabolic pathways in the body. Briefly, an enzymatic reaction occurs when catalyzed by the cytochrome P450 enzyme system, CYP2E1, converting ACR into glycidamide (GA). Studies have found that GA can combine with purine bases on deoxyribonucleic acid (DNA) molecules to form DNA adducts, inhibit the release of neurotransmitters, cause nerve terminal degeneration, damage nerve structures, and display distinct cumulative effects. In addition, the ability of GA to form Hb and DNA adducts is more significant than ACR. Therefore, it is believed that this pathway is the main route of ACR-induced neurotoxicity. (2) ACR undergoes biotransformation and is catalyzed by glutathione S-

transferase in the liver, combining with glutathione to generate N-acetyl-S-cysteine. It is further degraded into mercapturic ACR acids, which are excreted in the urine. This pathway is mainly responsible for ACR detoxification. Glutathione consumption reduces antioxidant levels, leading to excessive active oxygen accumulation and causing oxidative stress and neurotoxicity. Various reviews elaborate on the metabolic pathways of ACR. Those published by Koszucka et al. Rifai et al., and Fang et al. are recommended for more details.

Conclusion: Acrylamide (ACR), a potential neurotoxin, is produced by the Maillard reaction between reducing sugars and free amino acids during food processing. Over the past decade, the neurotoxicity of ACR has caused increasing concern, prompting many related studies.

Keywords: blood-brain , Acrylamide-Induced, Neurotoxicity

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The mystery of medical genetics; Duchenne disease (Review)

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Introduction: Neuromuscular disorders disrupt the function of muscles, motor neurons, peripheral nerves, and neuromuscular connections. The most common neuromuscular disorder and the most severe type of muscular dystrophy is Duchenne muscular dystrophy (DMD), which is caused by a mutation in the dystrophin gene. which is destroyed due to the production of dystrophin in the muscle. Muscles without dystrophin are more sensitive to damage and as a result, in addition to cardiomyopathy, muscle function is also lost. This disease is an X-linked disease and affects one in every 3,500 to 5,000 male births. In this article, we have discussed the various features of DMD as a comprehensive review.

Methods: Using the Google Scholar database, articles related to the topic were searched. The search time was selected from 2019 to today using the advanced settings of this database. After studying the found articles, these articles were discussed, categorized and reviewed based on different factors. Some phrases searched in Google Scholar include; Duchenne disease, genetics of Duchenne disease, clinical symptoms of Duchenne, new treatments for Duchenne, etc.

Results: History of disease discovery: The first person to describe this disease was Edward Merion. He studied the disease in 9 boys from 3 families and was able to point out some clinical signs of severe muscle wasting. For example, he noticed the enlargement of leg muscles in patients. Later, another scientist named Duchenne glioma investigated a wider spectrum of the disease, and in honor of his knowledge and efforts, the name of this muscular wasting disease, Duchenne, was chosen. Genetics of the disease: DMD is a genetic disorder caused by a mutation in the DMD gene. The DMD gene, located on the X chromosome, is the largest known human gene consisting of 79 exons that encode a 3685 amino acid protein called dystrophin. Since the discovery of the DMD gene in 1987, many different types of mutations have been identified. In a recent analysis, large mutations (affecting more than one exon) were identified in approximately 79% of patients, with large deletions accounting for 68% and large duplications responsible for the remaining 11%. 21% of the remaining patients have small mutations, half of which are nonsense mutations Although more than 99% of

patients with DMD have small deletions, duplications, or mutations, larger genomic rearrangements between an X chromosome and an autosome (non-sex chromosome) have been reported. Clinical symptoms and diagnosis: Delay in motor milestones, muscle weakness, hypertrophic calves, Gowers sign (Patients use their hands as support to stand). Cognitive impairment, speech delay, muscle spasms, scoliosis, bone metabolism disorder with mineral depletion. Ossification, visceral smooth muscle involvement, such as delayed gastric emptying and intestinal paralysis, constipation, and gastroesophageal reflux disease (GERD). treatment: For decades, scientists have been trying to find effective treatments for this tragic disease. Although there is no absolute cure for DMD, treatments that can delay the onset or slow the progression of the disease have been developed over the past few decades. Based on the mutation types, several strategies to target dystrophin repair have been proposed years ago and are currently under investigation (eg, premature termination codon mechanism, exon skipping, vector-mediated gene therapy, and myogenic cell transplantation).

Conclusion: DMD is known as a tragic disease because people with it usually have to be confined to a wheelchair by the age of 12. These people usually die in their third decade of life due to respiratory and heart problems. Considering that this disease does not have a routine and current treatment, it is suggested to pay more attention to the role of genetic counseling and prevention. Future research should clarify the advantages and disadvantages of new treatment methods for this disease.

Keywords: Duchenne muscle disease DMD

The needing of dentistry in patients with head and neck cancers (Review)

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Introduction: The risk of acute dental infections and life-threatening systemic infections during immunosuppression is greater in patients with chronic dental disease and poor oral hygiene. In the fight against odontogenic infections, oncology centers have applied an empiric approach, and the implementation of dental protocols for early cancer treatment was often involved. Fluoride therapy has been raised as a vital preventive way against caries following radiation and is effective in reducing the risk of dental caries in this special group. In addition, the benefits of using fluoride, observed initially in the common population, were extrapolated, and its helpful role in the treatment procedure of dental caries in people who received neck and head radiation was investigated. The main goal of this study is to search the entire literature for information on periodontal disease, dental caries, and precancerous tooth cleaning protocols in cancer patients receiving neck and head chemotherapy, radiation therapy, or cooperative treatment.

Methods: PubMed, Google Scholar, Scopus, and ScienceDirect are universally recognized databases that were used to retrieve published information (between 2000 and 2022). In the search strategy, published literature dealing with dental treatment procedures for cancer patients who have received neck and head radiotherapy and chemotherapy was downloaded and retrieved. Specific keywords such as “neck and head cancers”, “radiation therapy ”, “chemotherapy”, “dental follicle cells”, “precancerous lesions”, “fluoride therapy”, “head and neck cancers”, “radiation-induced xerostomia”, “xerostomia “ were used. 500 studies were funded. Based on abstracts, 470 studies were eliminated, and about 30 went for full-reading texts. Twenty-eight relevant articles with complete abstracts were included in the study.

Results: The article states that cancer patients who received neck and head radiotherapy were at higher risk of developing tooth decay during and after

treatment. The dental treatment included restorative, endodontic, extractive, and prophylactic procedures based on the clinician's assessment of the patient's clinical and radiographic condition, the time available before cancer treatment initiation, and the patient's immune status. The article also states that fluoride therapy was the best choice for the prevention of decay in these patients, and several studies have investigated the benefits of using fluoride for controlling the average of caries in the general population. In conclusion, cancer patients who underwent neck and head radiotherapy are at higher risk of caries development due to radiation-induced damage to the hole salivary glands in the oral cavity, which leads to the development of dry mouth or xerostomia.

Conclusion: Overall, managing the dental health of patients undergoing neck and head radiation therapy is a challenging and vital element of their overall healthcare and welfare. Dental treatment guidelines for these patients commonly encompass managing dental caries, administering root canal therapy if feasible, extracting non-viable teeth, and applying preventive dental care, often taking into account scaling and root preparation. The choice of dental treatment to be administered is contingent on multiple influences, for example, the assessment of the dental and radiographic state by the clinicians, the periodontal and pulpal status, the time remaining before cancer treatment initiation, and the immune condition of the patient.

Keywords: Cancer, Dental diseases, Dental caries, Precancerous dentistry

The only way to survive is with monosomy; Turner syndrome (Review)

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Introduction: As an illustrative and preliminary explanation about Turner syndrome, it can be said that the absence of X chromosome in women is the phenotype of Turner syndrome. But is Turner's syndrome seen only in the form of deletion of the x chromosome? No, this is not the case, we will read more detailed explanations. Turner syndrome, the only monosomy that can survive, is an attractive topic for research and investigation, so many researches have been written in this field on topics such as causes, genetics, symptoms and treatment. But the emptiness of an article with simple language and content classification in this field is felt, so the next article deals with this matter.

Methods: To write this article, we first reviewed the articles related to this topic in Google Scholar. We selected these articles from 2019 until now and then categorized and reviewed them. In this search, we used terms such as: Turner syndrome, Turner syndrome symptoms, Turner syndrome treatment methods, Turner syndrome genetics.

Results: The discovery of Turner syndrome is attributed to Mr. Henry Turner in 1938. The genetics of Turner syndrome is such that there is no x chromosome or it is incomplete, and to be more precise: the karyotype of Turner syndrome can be seen in different forms, the common point of all of them is the lack of x chromosomal material. including complete deletion of an x chromosome (45,x) or its mosaics 45,X/46,XX; 45, X/47, XXX)), the presence of p or q arm isochromosome, ring-shaped chromosomes, the presence of y chromosomal material and other complex cases. There are different types of Turner's syndrome states with different percentages in sufferers: about 40-50% of affected women have 45,x karyotype. 15 to 25% have mosaic state 45,X/46,XX and about 3% with 45,XX/46XY state and 20% as irzochromosome and also 10 to 12% have different amounts of Y chromosomal material. It is noteworthy that 99% of people with Turner syndrome (x45) spontaneously abort in the first trimester of pregnancy and only 1% of them are born. Although this number of people with Turner syndrome survive, they have the following symptoms: Short stature (about 20 cm shorter than normal), webbed neck, elbow deformity, late puberty, ovarian dysgenesis, infertility, congenital heart abnormalities, exocrine gland

disorders, diabetes, osteoporosis, and autoimmune disorders. Turner syndrome also affects people's relationships. Sufferers usually have delayed social and emotional development and have problems in social understanding. These problems affect the ability of these women to adapt to society's demands, such as marriage, etc. In the field of Turner's syndrome treatment, growth hormone is usually used to increase height (even in adults), and in addition, the use of estrogen is also necessary to induce puberty. Also, various researches are being conducted in the field of having children of these people.

Conclusion: In this article, we have tried to provide the basic information required for any researcher who wants to have comprehensive information about Turner syndrome. In the next articles, it is better to address issues such as the treatment of this disease with new methods such as gene therapy, etc. better and more widely. Also, to improve the treatments that are done today, such as hormone therapy, by raising questions such as when is the best time for hormone therapy or what is the best method for quick and timely diagnosis of this disease.

Keywords: Turner syndrome. Genetics . X chromosom

The Potential Revolution of Cancer Treatment with CRISPR-Cas9 (Review)

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Introduction: Cancer is one of the leading causes of disease-associated mortality with rising incidence worldwide. Simultaneously, advances have been made in the prevention and treatment of many types of cancer, which result in prolonged survival or even cures. Existing means in clinical treatment of cancer, including surgery, chemotherapy and radiotherapy, can cause certain effects. CRISPR/Cas9 is a prokaryotic, adaptive immune system that consists of a programmable RNA molecule that helps guide an associated Cas9 endonuclease to specific exogenous genetic invaders based on recognized sequences. Powerful genome-editing technology known as Clustered regularly interspaced palindromic sequences-acronym CRISPR, is now eclipsing all other genome-engineering techniques. This revolutionary technique allows researchers to accomplish targeted manipulation in any gene (DNA sequence) in the entire genome of any organism in vitro or now even directly in endogenous genome, thus helping to elucidate the functional organization of genome at systems level and identifying casual genetic variations.

Methods: In the current study, keywords including CRISPR-Cas9, Cancer, and Treatment were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized. The searches comprised all published paper from 2000 to 2022. All of full text was considered and the papers manifested as only abstract was excluded. The full papers selected that specific effect on cancers only. Totally 50 papers were selected and studied in this review.

Results: CRISPR plays a vital role in detection of cancers. The CRISPR-Cas9 system evolved as an immune defense against foreign bacteriophage or plasmid infection in bacteria or archaea. Genome editing by CRISPR-Cas9 system for production of the chimeric antigen receptor (CAR) has been broadly recognized as one of the largest progress in personalized cancer

immunotherapy. A recent clinical trial 38 showed that autologous reintroduction of CD4T cells whose CCR5 (CC chemokine receptor 5) gene was inactivated in vitro by ZFN was safe and lead to decreased viral load, lending support to the potential of CRISPR-Cas9 in Acquired immunodeficiency syndrome (AIDS) gene therapy. Articles show CRISPR-Cas9 editing system is derived from bacterial native immune system and hence has inherent advantage in defense against or clearance of viral infection that are associated with carcinogenesis, such as HBV and hepatitis C virus in liver cancer, Epstein-Barr virus (EBV) in nasopharyngeal carcinoma and human papillomavirus (HPV) in cervical cancer. The primary CRISPR/Cas9 clinical trial in China is editing T cells from patients with CRISPR/Cas9 system in vitro and transplanting these altered cells back into the patients to upgrade the tumor treatment effect. Other articles demonstrated catalytically inactive dCas9 can be recruited by gRNAs to specific target DNA sites, and when fused to transcriptional activation or inhibition domains, can be exploited to activate or repress specific target genes. The approach is based on CRISPR/Cas9-mediated PD-1 gene deletion in T-cells ex vivo and their reintroduction into patients, where the gene-deleted T-cell will home to the tumor and activate the immune response with the possibility of tumor eradication.

Conclusion: In conclusion, the RNA-guided genome editing tool CRISPR-Cas9 offers several advantages over protein guided counterparts and RNAi techniques. It has shown therapeutic potentials in cell lines or animal models for infectious diseases, monogenic diseases and cancer so CRISPR plays a vital role in detection of cancers.

Keywords: CRISPR-Cas9, Cancer, and Treatment

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The Protective Effect of Niosomal Hesperidin on M1/M2-Macrophage Polarization-Based Hepatotoxicity in Chlorpyrifos -Induced Toxicities (Research Paper)

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Introduction: The organophosphate pesticide chlorpyrifos (CPF) can cause developmental, neurological deficiencies, and mitochondria-mediated oxidative stress responses. Natural products show notable features such as unusual chemical variety, chemical and biological possessions with low toxicity. These properties make natural products the pioneers in discovering new drugs .Where in modern agriculture, the use of pesticides is essential to develop the quality of the crops, but the unidentified effects on the on vital organs lead scientists to more investigations on the therapeutic agents for decreasing side effects. Therefore, in the present study, nanoliposomes were designed for the delivery of hesperidin to evaluate the ameliorative role and its effect against oxidative stress, lipid peroxidation, and tissue lesions in the mice received CPF.

Methods: In this study, the effect of niosomal hesperidin (Nio+Hesp) prepared by thin film hydration method on the polarization of M1-M2 liver macrophages and the amount of inflammatory cells secretion in the brain, liver, and ovary tissues of CPF induced mice (3 mg/kg for 4 weeks; Intraperitoneally) was investigated. Fourty C57 mice were divided into CPF, Sham, CPF+Hesp, and CPF+Nio+Hesp groups and treated carried out orally for 30 days. The activity of superoxide dismutase (SOD) and malondialdehyde (MDA), tissue changes, inflammation, and apoptosis in brain, liver, and ovary tissues, the number of ovarian germ cells, and M1-M2 liver macrophage polarization were evaluated by examining the expression of CD163 and CD68 genes.

Results: Nio+Hesp prescription caused an increase in SOD and a decrease in MDA. Nio+Hesp decreased the amount of cell apoptosis in the liver, also reduced the expression of CD163 and CD68 genes. Although there was a significant difference between Hesperidin and Nio+Hesp in the increase of Graafian follicles, corpus luteum, and peri-antral follicles, no substantial

difference was observed in primary follicles in the uterus. Both Nio+Hesp and Hesp alleviated CPF-induced hepatotoxicity, however, Nio+Hesp was superior to Hesp in downregulation of the CD163 and CD68 genes expression.

Conclusion: In this study, hesperidin, an antioxidant and anti-inflammatory agent, and niosomal hesperidin effect on CPF induced toxicity effects were studied for the first time. The obtained results from this study showed that niosomal hesperidin can have significant antioxidant effects in mice treated with chlorpyrifos by effects on the polarization of M1-M2 liver macrophages and the amount of secretion of inflammatory cells in the brain, liver and ovarian tissue. Therefore niosomal hesperidin could be used as a novel agent in the treatment of organs injury due to CPF toxic effects. However, further studies are needed to verify these results.

Keywords: Chlorpyrifos. Hesperidin. Niosomal Hesperidin. Antioxidant

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The p[V230A]; [V230I] genotype was detected in a 32 years old normal adult with untreated mild hyperphenylalaninemia (Research Paper)

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Introduction: Phenylketonuria (PKU) is a hereditary disorder caused by phenylalanine hydroxylase enzyme (PAH) defects that might cause severe brain damage. The current main treatment, dietary management, can prevent the symptoms if commenced early. However, it has side effects if used for a long time. According to recent guidelines, treatment is not required for patients with mild hyperphenylalaninemia (mHPA) and Phenylalanine level <360 µmol/l. Since the correlation between genotype and metabolic phenotype has been demonstrated earlier, genotype-based detection of patients who do not need treatment might help with genetic counseling and choosing the most appropriate treatment option.

Methods: Genetic analysis was conducted for a family containing a child suffering from PKU and her parents. The level of serum Phenylalanine was assessed in subjects who carried two pathogenic variants within the PAH gene. Both of pathogenic variants detected in the normal adult with untreated mHPA were computationally analyzed to assess their pathogenicity.

Results: The affected child and her mother were bearing p.[V230A];[V230A] and p.[V230A];[V230I] genotypes respectively. The mother had 179 µmol/l serum Phenylalanine level, so she was a normal adult with untreated mHPA who had never taken any medical intervention to control or lower her serum Phenylalanine level. Both detected variants were pathogenic and affected the catalytic domain of the PAH enzyme diversely

Conclusion: The p. V230I pathogenic variant was demonstrated to be responsible for the mHPA phenotype in the normal untreated adult detected in this study.

Keywords: Normal adult, PAH, untreated mHPA, Phenylalanine, genotype

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The Relationship between Eating Speed and the Risk of Metabolic Syndrome (Review)

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Introduction: Metabolic syndrome (MetS) is a complex disorder characterized by high blood pressure, abdominal obesity, dyslipidemia, and impaired blood glucose and insulin metabolism. This disorder increases the risk of ovarian cysts, fatty liver, sleep disorders, asthma, gallstones, type 2 diabetes, cardiovascular diseases, and some cancers. We sought to explore the association between eating speed and the risk of MetS in the present review article.

Methods: Multiple databases including PubMed, Scopus, and Web of Science as well as Google Scholar search engine were searched using appropriate keywords up to the middle of 2023. The keywords used were “metabolic syndrome” or “MetS” and “eating speed”.

Results: Two cross-sectional studies found no significant association between fast or slow eating and the risk of MetS. However, eight cross-sectional studies and one cohort study reported that fast eaters had a significantly higher risk of developing MetS than slow eaters. Two studies have even shown that the risk of MetS was significantly increased in fast eaters than moderate-speed eaters. In addition, the results of a cohort study found a significant reduction in the risk of MetS in adults with slow eating speed. Fast eating speed seems to increase the risk of developing MetS through overeating and extra energy intake, impaired satiety signaling, poor nutrient absorption, causing insulin resistance, and dysregulation of gut microbiota.

Conclusion: It seems that eating slowly is a simple, inexpensive, and practical strategy to reduce the risk of MetS and its consequences. Nevertheless, interventional studies should be designed to establish the relationship between eating speed and the risk of MetS.

Keywords: Metabolic Syndrome, Eating Speed, Fast Eaters, Slow Eaters

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The relationship between serum zinc concentration and metabolic syndrome in HTLV-1 infected subjects (Research Paper)

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Introduction: Chronic Systemic inflammation is a probable factor that promotes the interplay between human T-lymphotropic virus type 1 (HTLV-1) infection and metabolic syndrome (Mets), and thus contributes to the progression of both. According to available evidence, Zinc (Zn) is one of the essential trace elements which can reduce inflammation and oxidative stress. In this study, we aimed to investigate the concentration of serum zinc and its association with metabolic syndrome among HTLV-1-infected individuals.

Methods: In this study 271 HTLV-1 infected subjects were divided into two groups, 154 with Mets and 117 without Mets according to IDF criteria. Serum zinc concentration was measured by flame atomic absorption. SPSS version 18 was used for data analyzing.

Results: The serum levels of zinc were significantly lower in individuals with Mets ($p < 0.05$). The body fat percentage (FAT) and serum high-sensitivity C-reactive protein (hs-CRP) were significantly higher in individuals with Mets ($P < 0.001$ and $P = 0.025$, respectively); whereas, no significant changes were seen in superoxide dismutase (SOD). According to multiple logistic regression analysis, after adjusting for age, sex, hs-CRP, and FAT, the risk of MetS in the quartiles 1,2 and 3 was 2.477 (1.298-4.726) compared to the 4th quartile.

Conclusion: Conclusion: Our finding pointed to a significant association between serum concentration of zinc and the prevalence of metabolic syndrome (Mets) among individuals with HTLV-1 infection. Thus, regular screening for zinc intake and its serum levels may help HTLV-1 infected individuals reduce the risk of metabolic syndrome and prevent its subsequent complications.

Keywords: HTLV-1, zinc, metabolic syndrome

The Role and Therapeutic Targeting of JAK/STAT Signaling in Glioblastoma (Review)

Ghazal Azizi,[1,*]

1.

Introduction: Due in great part to its diffuse infiltrative nature, molecular heterogeneity, and immunological escape ability, glioblastoma continues to be one of the deadliest and treatment-refractory human cancers. Proliferation, anti-apoptosis, angiogenesis, stem cell maintenance, and immunological suppression are just a few of the protumor-genic actions that the Janus kinase/signal transducer and activator of transcription (JAK/STAT) signalling pathway significantly supports. We discuss the present level of knowledge about the therapeutic options, future directions for the field, and the biological function of JAK/STAT signaling in glioblastoma. The aim of this study was to investigate The Role and Therapeutic Targeting of JAK/STAT Signaling in Glioblastoma.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The STAT family of transcription factors is comprised of seven proteins—STAT1, STAT2, STAT3, STAT4, STAT-5a, STAT-5b, and STAT6—which reside in the cytoplasm and are activated by phosphorylation as a downstream consequence of a number of signalling pathways, including cytokines, growth factors, or non-receptor tyrosine kinases. In the classical JAK-mediated pathway, cytokine binding of its cognate receptor leads to receptor dimerization followed by docking of JAK and consequent phosphorylation of the receptor's cytoplasmic tail. STAT proteins are then recruited via their SH2 domains to the activated receptor where tyrosine phosphorylation occurs, STAT hetero- or homodimerization ensues, and activated STAT then undergoes translocation to the nucleus to bind DNA elements such as promoters or enhancers to both, directly and indirectly, regulate transcription of associated genes. Although tyrosine phosphorylation of STAT is the most important activating step, STAT can be phosphorylated on serine residues to modulate their activity. To date, a vast number of agents ranging from antisense oligonucleotides and repurposed drugs, JAK1/2 to direct STAT3 inhibitors have been the subject of investigation in numerous cancers. Targeting aberrant upstream IL-6/IL-6R signaling is one potential avenue of JAK/STAT blockade. Treatment with IL-6 pathway blockade via its receptor (IL-6R, tocilizumab) or binding soluble IL-6 (siltuximab) has been

shown to inhibit glioma growth in vitro and reduce the expression of coinhibitory molecules such as PD-L1 on infiltrative myeloid cells. A number of repurposed pharmacologic agents have been found to have STAT3 inhibitory activity; however, off-target effects due to lack of specificity and questionable CNS penetrance have limited their utility. Atovaquone is an anti-malarial drug FDA-approved for pneumocystis pneumonia that was found to have STAT3 inhibitory effects; notably, it appears to be poorly bioavailable in the CNS. Arsenic trioxide (ATO) was shown to reduce STAT3 activation via JAK inhibition and induce apoptosis and stemness of GSCs. Despite encouraging safety data, a phase II trial combining ATO with radiation and temozolomide for newly diagnosed malignant glioma did not demonstrate a survival benefit.

Conclusion: Sorafenib, a multi-kinase (Raf, VEGFR2, and PDGFR-) inhibitor with STAT3 inhibitory activity that has been FDA-approved for treating other solid tumors, was demonstrated to reduce the growth of GBM in vitro, most likely due to its effects on AKT and MAPK. For patients with newly diagnosed or recurrent GBM, later clinical trials combining sorafenib with temozolomide, radiotherapy, or mTOR inhibition failed to show a survival benefit.

Keywords: JAK/STAT, Signaling, Glioblastoma

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The role of AGER in the P13K-AKT and JAK-STST signaling pathway and the direct relationship between decreased expression and decreasing mortality in lung cancer (Research Paper)

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Introduction: Lung cancer is the major cause of cancer mortality worldwide. The most common type of lung cancer is non-small cell lung cancer, which consists of three tissue subtypes LUAD, LUSC, and large cell lung carcinoma. The advanced glycosylation end product (AGE) receptor encoded by this gene is a member of the immunoglobulin superfamily of cell surface receptors [1][2][3][4] .

Methods: The GSE168466 dataset has been found in the GEO online database. Was examined the interaction between mRNA and lncRNA using lncRRIsearch. With miRWalk, we investigated miRNA mRNA interactions using all miRNAs recovered from DIANA-Tar Base v.8. Additional databases include KEGG, Reactome, and STRING. Comparing the expression of genes in lung cancer was explored by Gepia2 databases. The expression of lncRNAs in different tissues has been examined by the lnCAR databases. This result was also confirmed by GEPIA2 and ENCORI. Gene ontology was checked using the Enrich R database.

Results: AGER was selected as a significantly up-regulated gene (logFC=3.1, adj. Pvalue=7.81e-22) in tumor samples compared to normal samples from NSCLC Tissue. survival analysis showed a significant direct relationship between down expressed and decreasing mortality (Log-rank p=0.002 HR (high)=0.62 p(HR)=0.0023). According to the analysis, a potential ceRNA network between AGER, hsamiR-509-3P, and HELLPAR-001 can be established. The involvement of AGER in the DNA mismatch repair pathway can fortify the possibility of the importance of AGER in changing non-malignant cells into cancer cells and AGER plays an important role as a receptor in AGE-RAGE signaling pathway in diabetic complications with an effect on P13K-AKT signaling pathway which lead to Apoptosis as well as it can by JAK-STST signaling pathway impress on vascular remodeling.

Conclusion: We identified the hub lncRNA-mRNA network involved in regulating various biological processes from NSCLC Tissue. Interaction analysis of AGER, hsamiR-509-3P, and HELLPAR-001 illustrated to have a single local base-pairing interaction. in cervical cancer. Moreover, AGER by using the P13K-AKT signaling pathway causes Apoptosis and also with such an effect on the JAK-STST signaling pathway would be able to regulate vascular remodeling.

Keywords: Lung cancer (LC), JAK-STST signaling pathway, Apoptosis, P13K-AKT signaling pathway, ceRNA network

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The role of artificial intelligence in the diagnosis of lung cancer through thoracic imaging techniques: advantages and challenges (Review)

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Introduction: A prevalent malignant tumor illness with significant mortality and clinical impairment rates is lung cancer. Currently, manual pathology section analysis is the primary method used to detect lung cancer, although this method is inefficient and vulnerable to error due to its subjective character. There are several imaging techniques to diagnose lung cancer, such as computed tomography (CT) scan, Magnetic resonance imaging (MRI) scan, and chest X-ray. Considering the high rate of false positives and negatives, human error in the interpretation of images, low speed of analysis of results in emergencies, and low accuracy in these methods, it seems that we need auxiliary methods to solve these defects. With the ongoing development of technology, artificial intelligence (AI) has gradually been included in imaging diagnosis, and it has the potential to improve the effectiveness of lung cancer screening. Several studies in this field have been conducted on several imaging methods, which will be comprehensively reviewed. This review deals with the question of whether artificial intelligence has sufficient sensitivity and specificity to outperform human experts in diagnosis. Also, this study aims to express the advantages and problems of artificial intelligence as a tool for better analysis of imaging results.

Methods: This article is written as a review. A specific search strategy was determined based on keywords and their synonyms. Then the articles were extracted by searching Google Scholar and PubMed databases. Keywords included lung cancer and artificial intelligence, and only primary studies including interventional and observational were studied. The obtained articles were filtered based on specific inclusion and exclusion criteria and qualitatively reviewed. Finally, the results of the selected articles were reported by mentioning the methodology and main findings of the study.

Results: Based on the results, the diagnostic system with the help of artificial intelligence for imaging techniques has a significant diagnostic accuracy (with p value less than 0.05) for the diagnosis of lung cancer, which has a significant value for the diagnosis of lung cancer and more possibility to realize the development application in the field of clinical diagnosis. Therefore, AI with intelligent learning algorithms and high accuracy can detect imaging

findings that are usually missed. However, there is a margin of error and the clinical utility of AI has yet to be fully proven.

Conclusion: AI has surfaced as a highly promising instrument to aid radiologists in the examination of thoracic images for the detection of lung cancer. The advantageous features of AI comprise the proficiency to expeditiously process copious amounts of data, detect subtle anomalies that may elude human observers, and provide quantitative measurements for precise diagnosis. Furthermore, AI algorithms exhibit the capability to acquire knowledge from vast amounts of data and progressively elevate their efficiency over a period of time. Several matters necessitate resolution to effectively employ artificial intelligence in the identification of lung cancer. To train AI models, for instance, one needs high-quality annotated datasets. Other requirements include ensuring the robustness and generalizability of algorithms across various populations and imaging modalities, as well as addressing moral and legal issues and gaining acceptability.

Keywords: Lung Neoplasms, artificial intelligence, AI-assisted diagnosis, thoracic imaging techniques

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The Role of Copper and Cuproptosis in Colon Cancer Development and Treatment (Review)

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Introduction: Colon cancer is one of the leading tumors and the third most common type of cancer globally; it is considered one of the major killers. One of the cancer detection methods is using copper metal because metastasized cells need more copper for survival. Cuproptosis is a different type of cell death from copper and the accumulation of acidified lipids, unlike traditional cell death cause. Cuproptosis, as an essential cellular function and process, has been recently discovered and can play a significant role in the treatment of colon cancer.

Methods: Articles and information from 2010 to 2023 were searched using the keywords "colon cancer," "cuproptosis", and "copper" in scientific databases like PubMed, Scopus, and Google Scholar.

Results: Copper homeostasis plays an essential role in the development of various tumors, and its imbalance can lead to cytotoxicity, which affects the growth and proliferation of cancer cells. By changing its form in cuproptosis, binding to fatty acids, and changing its shape, copper causes the loss of iron-sulfur cluster proteins and cell death. Also, the expression level of genes involved in cytolytic activity, checkpoint, and para-inflammatory pathways in colon cancer patients has increased significantly, which indicates the critical role of immune dysfunction in cuproptosis and prognosis of colon cancer patients.

Conclusion: Considering the lethality of colon cancer and the high number of victims in the world, as well as the more precise identification of the relationship between the effect of cuproptosis and the immune system response in colon cancer, manipulating copper levels and cuproptosis pathways may offer new strategies for colon cancer treatment and, we also need more detailed and complete studies for more effective treatments.

Keywords: Cuproptosis, Colon cancer, Copper, Cell death, and infection.

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The Role of Diffusion Tensor Imaging (DTI) in the Diagnosis and Evaluation of Spinal Cord Injury (Review)

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Introduction: Spinal Cord Injury (SCI) is a widespread problem influencing approximately 18,000 individuals annually in the United States. In this clinical syndrome, the structure and function of the spinal cord are damaged via disease or injury which can lead to disruption in the normal physiology of the autonomic nervous system. It is critical to have a quantifiable measure to assess SCI histopathology. Although Conventional Magnetic Resonance Imaging (MRI) can provide anatomic information about the brain and spinal cord, it cannot detect subtle changes that occur in SCI. This issue led to the utilization of Diffusion Tensor Imaging (DTI), a novel nonionizing imaging technique that has a high sensitivity in recognizing the microstructures occurring in SCI. DTI's main principle is the measuring of water molecule's diffusion. The fat content in white matter results in more diffusion in comparison to the gray matter which is more made of cell bodies with small orientation. The purpose of this article is to investigate the potential utility of DTI in the diagnosis and possible prognosis of SCI.

Methods: This Search was conducted in the Google Scholar and PubMed databases using the keywords: DTI AND Spinal Cord Injury published since the year 2022. After the Screening of the title and abstract of the articles, The Related articles were assessed and included based on their relevance to the main purpose of this review. The Irrelevant articles and the animal studies were excluded from our review. Some of the references to the relevant articles were also added in this review. The most important parameters measured in DTI include Fractional anisotropy (FA), Mean diffusibility (MD),

Radial diffusibility (RD), and Axial diffusibility (AD). These parameters provide details on the pathophysiological changes in SCI.

Results: Our Search resulted in 2070 articles that were narrowed to 41 articles based on the inclusion criteria. The parameters of DTI vary significantly in the location of the injury. With respect to the severity of the spinal cord injury, the value of FA decreases significantly compared to healthy individuals. Meaning the lower the FA value, the worse the clinical condition of the disease. Also, asymmetric FA values can indicate laterality in the neuropathology of SCI. Generally, the MD values increase in patients with acute SCI. Higher MD values correlate to more severe clinical conditions. In most studies, it has been shown that with the injury of the axon, the AD values decrease but in contrast, the RD values increase.

Conclusion: In multiple studies, the observed changes in the DTI parameters can with high accuracy point to axonal damage or functional disruption to the spinal cord. This review reports the important usefulness of DTI in evaluating the pathological microstructures arising in the SCI.

Keywords: Diffusion Tensor Imaging, Spinal Cord Injury, Magnetic Resonance Imaging

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The role of gene polymorphisms in brain tumor pathogenesis and its implications for personalized medicine (Review)

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Introduction: Brain and other nervous system cancer is the 10th leading cause of death for men and women. Various genetic factors play an important role in the occurrence of brain tumors,and among these genetic factors, there are polymorphisms that are more important than others, and in this review article, we have discussed the role of these polymorphisms in brain tumor pathogenesis and its implications for personalized medicine.

Methods: An advanced literature search was conducted in PubMed, Google Scholar and Embase databases. Searching was included following keywords: brain tumor, gene polymorphism,personalized medicine. All the articles since 2000 was included in the present study.

Results: Polymorphisms of the ALAD(G177C), TERT(rs2853676) , EGFR(rs4947986), TP53(Arg72pro) genes are the most important genetic factors behind brain tumor pathologies which allowing for tailored treatment strategies and improved prognostic assessments

Conclusion: Considering found significant gene polymorphisms not only can identify predisposed individuals at earlier stages, but also can be implicated in the targeted therapy and follow up of the brain tumor patients.

Keywords: brain tumor, gene ,polymorphism,personalized medicine , gene variant, tumor grade

The Role of Gut Microbiomes in Breast cancer (Review)

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Introduction: Breast cancer (BC) stands as the prevailing form of invasive cancer among the female population worldwide, impacting approximately one out of every seven women throughout their lives. In the year 2022, a considerable number of women, amounting to around 287,850 individuals, were diagnosed with BC. Furthermore, an additional count of approximately 51,400 women were diagnosed with the specific condition known as breast ductal carcinoma in situ. BC presents itself as a disease with diverse characteristics and complexities, exhibiting significant heterogeneity between individual tumors as well as within tumors themselves. Research on risk factors for cancer has demonstrated that microorganisms can play a role in the progression of cancer in approximately 15 to 20 percent of instances. The microbiome present in our gastrointestinal tract possesses the ability to generate various metabolic substances that safeguard the equilibrium of the host. However, in cases of an imbalance in the gut flora, these microorganisms can also generate harmful molecules that have the potential to induce inflammation and the development of cancer. In this review article, we discuss the role of gut microbiota in BC. The gastrointestinal tract environment is known as an intricate ecosystem called the gut microbiota, consisting of various microorganisms such as bacteria, archaea, fungi, viruses, and protozoa. Increasing evidence suggests that the microbial community residing in the gastrointestinal tract is of significant importance to the overall human health. Moreover, when this community is disrupted and its balance is disturbed, it has been linked to numerous abnormal physiological processes.

Methods: Read more than 20 articles from 2020 onwards in the field of the gut microbiome and its role in modulating developing and treating breast cancer.

Results: Studies show that gut microbiota plays a role in BC. Also, the regulation of microbiota may help to predict the risk of BC. Intestinal

metabolites have potential anticancer activity against BC. The potential anticancer effects of butyrate, a short-chain fatty acid, have been investigated in various cancer types, such as BC. Its ability to inhibit cancer growth has been observed through diverse molecular pathways. Similarly, Nisin a type of bacteriocin, has displayed a variety of anticancer characteristics, particularly about cancers of the gastrointestinal tract. Though the evidence is limited, there is some support for its potential application in the treatment of BC. Comparatively, in recent investigations, inosine, a naturally occurring purine nucleoside, has exhibited potential as a natural agent for combating cancer, even though its comprehensive exploration in this context remains incomplete. Moreover, recent research has indicated that the effectiveness of conventional chemotherapeutic agents can be affected by metabolites produced by gut microbiota, thereby suggesting the potential integration of these metabolites into combination therapies. Other studies showed that patients with BC and benign breast lesions have significant changes in the gut microbiota. Porphyromonas and Peptoniphilus are more abundant in BC patients, while Escherichia and Lactobacillus are more abundant in patients with benign breast lesions. Microbiota can affect estrogen levels and increase BC. Knowing the gut microbiota can lead to new treatments.

Conclusion: Throughout numerous studies, substantial evidence has been accumulated which substantiates the essential contribution of the intestinal microbiome in safeguarding overall well-being and averting detrimental transformations, such as the development of cancer. BC continues to pose a severe health risk worldwide, and existing approaches to treating breast tumors are encumbered by various limitations and resistance to therapy, thereby constraining their effectiveness in therapy. While there is still much to comprehend regarding the correlations between gut microbiota and BC, the disruption of the gut microbiota has been acknowledged as a pivotal factor in the inception, advancement, evolution, and spread of breast carcinoma. This issue requires more research and more comprehensive clinical studies to determine more precise connections and more specific mechanisms between the gut microbiome and BC.

Keywords: Breast Cancer, Microbiome, Microbiota, Metabolite

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The role of human papillomavirus vaccines And treatment in cervical cancer review article (Review)

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Introduction: Viral infections are responsible for 15-20% of human cancers. Infection with oncogenic viruses can increase different stages of carcinogenesis. HPV is the most common sexually transmitted infection (STI), and about 15 types are associated with cancer. Despite effective screening methods, cervical cancer remains a major public health problem. Continuous human papillomavirus infection is the main cause of cervical cancer, which is the main cause of cancer-related deaths among women worldwide. The best strategy to reduce the incidence of cervical cancer is through the administration of HPV vaccines along with routine cervical screening. The HPV vaccine is very important for public health. The present study aims to investigate the role of the vaccine in preventing HPV and cervical cancer.

Methods: Clear evidence from randomized trials and population-based studies suggests that vaccination against human papillomavirus reduces the incidence of cervical cancer. At present, 3 types of vaccines have been introduced, the 4-strength Gardasil vaccine is more recommended. Studies show that the vaccine causes cervical cancer.

Results: Developed countries have reduced the challenge of cervical cancer by introducing structured screening programs and recently the HPV vaccine. Countries that have successfully introduced national HPV vaccination programs are on track to eliminate cervical cancer within the next few decades.

Conclusion: This summary deals with the main causes of cervical cancer, high-risk strains of HPV, and this type of malignancy can be prevented. Knowledge of HPV prevalence and type of distribution can help in the successful implementation of the vaccination program.

Keywords: Cervical cancer, vaccination, cervical cancer screening, HPV vaccination, Prevention, papilloma

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The role of IL-1 family of cytokines and receptors in pathogenesis of COVID-19 (Review)

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Introduction: A global pandemic has erupted as a result of the new brand coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This pandemic has been associated with widespread mortality worldwide. The antiviral immune response is an imperative factor in confronting the recent coronavirus disease 2019 (COVID-19) infections. In the meantime, cytokines are recognized as crucial components in guiding the appropriate immune pathways in restraining and eradicating the virus. Moreover, SARS-CoV-2 can induce uncontrolled inflammatory responses characterized by hyper-inflammatory cytokine production, which causes cytokine storm and acute respiratory distress syndrome (ARDS).

Methods: As excessive inflammatory responses contribute to the severe stage of the COVID-19 disease, the pro-inflammatory cytokines are regarded as the Achilles heel during COVID-19 infection.

Results: Among these cytokines, interleukin (IL-) 1 family cytokines (IL-1, IL-18, IL-33, IL-36, IL-37, and IL-38) appear to have a solid inflammatory role in severe COVID-19.

Conclusion: Hence, understanding the underlying inflammatory mechanism of these cytokines during infection is critical for reducing the symptoms and severity of the disease. Here, the possible mechanisms and pathways involved in inflammatory immune responses are discussed.

Keywords: Infammation

The Role of Immune Cells and Its Antibodies Against SARS-Cov-2 Infection (Review)

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Introduction: The SARS-CoV-2 pandemic has demonstrated the importance of studying antiviral immunity within sites of infection to gain insights into mechanisms for immune protection and disease pathology. As SARS-CoV-2 is tropic to the respiratory tract, many studies of airway washes, lymph node aspirates, and postmortem lung tissue have revealed site-specific immune dynamics that are associated with the protection or immunopathology but are not readily observed in circulation. This study investigates The role of immune cells and their antibodies against SARS-CoV-2 infection

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed for investigating The role of immune cells and their antibodies against SARS-CoV-2 infection.

Results: Almost everyone with SARS-CoV-2 infection seroconverts within 2 weeks post-symptom onset (PSO), producing IgM and IgG antibodies that predominantly recognize the viral spike and nucleocapsid proteins. However, high serum titers of total or neutralizing antibodies against SARS-CoV-2 are more frequently found in severe cases of COVID-19 and do not necessarily correlate with better disease outcomes of the primary infection. Transfusion of convalescent plasma was initially reported to be able to reduce the mortality rate of people hospitalized with COVID-19, although increased survival was not replicated in a subsequent large controlled trial. Neutralizing antibodies that block angiotensin-converting enzyme 2 (ACE2)-dependent viral entry into host cells correlate well with the efficacy of prophylactic vaccines. Serum levels of neutralizing antibodies to SARS-CoV-2 peak within the first few weeks after infection or vaccination and decline subsequently, leading to reduced protection and an increased risk of re-infection by the original strain or newly emerging variants of concern or interest (VOCs or VOIs). Vaccine booster shots can induce broader and more potent neutralizing antibodies in patients convalescing from COVID-19 compared with previously uninfected individuals. Antibodies that are cross-reactive because of previous exposure to other pathogenic and seasonal coronaviruses may affect the development of SARS-CoV-2-specific neutralizing antibodies as well. What emerges from these and other studies of humoral immunity to SARS-CoV-2 is the

importance of the timing and context in which B cell activation and antibody responses are initiated and maintained.

Conclusion: More studies and continuous monitoring of ADE are warranted, because in principle cross-reactive antibodies from previous coronavirus infection could exacerbate SARS-CoV-2 infection and, as new VOCs continue to emerge, neutralizing antibodies against earlier strains may lose neutralizing potency and become capable of mediating ADE instead. This latter point is important from a vaccination perspective because vaccines appear to induce more binding antibodies than neutralizing antibodies, compared with natural infection.

Keywords: Immune Cells, Antibodies, SARS-Cov-2, Infection

The role of JAK/STAT signalling in the cancer (Review)

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Introduction: The JAK/STAT system controls the maintenance of stem cells, hematopoiesis, and the inflammatory response in addition to controlling embryonic development. Through several transmembrane receptor families, the route transmits signals from cytokines, interleukins, and growth factors. Erythropoietin and granulocyte colony-stimulating factor (G-CSF) receptors are examples of type I receptors. Granulocyte-macrophage colony-stimulating factor receptors are type IIa receptors, and interleukin-6 and leukaemia inhibitory factor receptors are members of the type IIb subfamily. These receptors' intracellular tails are inherently linked to janus kinases (JAKs), dormant kinases. The phosphorylation of certain tyrosine residues in receptor-associated JAKs, which occurs as a result of ligand interaction, transforms inactive JAKs into catalytically active JAKs. Ligand binding produces conformational changes in receptors that alter the alignment of receptor-associated JAKs, enabling phosphorylation of specific tyrosine residues that convert inactive JAKs into catalytically active tyrosine kinases. The aim of this study was to investigate The role of JAK/STAT signalling in cancer.

Methods: This review study has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Increased expression of the G-CSF receptor is observed in high-grade ovarian epithelial tumours, and experiments in cell culture suggest that G-CSF contributes to JAK/ STAT activation in this disease.Gain-of-function mutations in JAKs have been observed to cause pathway activation in haematological malignancies. More recently, large-scale sequencing efforts have identified genetic changes affecting JAKs in certain solid tumours. Missense mutations in JAK1 have been identified in 9% of patients with Hepatitis B-associated hepatocellular carcinoma, and validation in cell culture shows that these mutations increase phosphorylation of JAK1 and STAT3 and enable cytokine-independent growth. In gastric adenocarcinoma, a comprehensive molecular characterisation project has revealed frequent amplification of the chromosomal locus containing JAK2. Corresponding increases in JAK2 messenger RNA suggest that this may increaseJAK2 protein levels and pathway activity. Activating mutations in STATs, although generally rare, have been described in cancer. In large granular lymphocytic

leukaemia,40% of patients have mutations affecting the SH2 domain of STAT3. These introduce hydrophobic residues thought to stabilize STAT dimers, and lead to increased STAT-responsive transcription. Amplification of the STAT5A/B locus has been described in prostate cancer, and is associated with increased expression and nuclear localisation of STAT5 in tumour samples. These amplifications increase cell survival in culture and promote tumour growth in a xenograft model.Reduced expression of negative regulators can cause increased pathway activation. In non-small cell lung cancer (NSCLC) tumour samples, expression of SOCS3 is lost due to promoter hypermethylation, an epigenetic change that reduces gene transcription.The impact of this on pathway activation was validated using a NSCLC cell line, where restoration of SOCS3 expression reduced constitutive STAT3 phosphorylation (He et al, 2003). The PIAS3 protein levels have been shown to be reduced in glioblastoma, possibly due to increased protein degradation. In glioblastoma tissue samples, low levels of PIAS3 are associated with increased pSTAT3 and increased expression of proteins produced from STAT target genes.

Conclusion: The JAK/STAT signaling system is very active in many solid tumors, according to a direct study of tissue samples. Since JAK/STAT signaling plays a crucial role in a network of signaling pathways that are dysregulated in cancer, it is possible to use targeted suppression of JAK/STAT signaling as a therapeutic strategy to treat patients with solid tumours. Targeting JAK/STAT activation inhibitors at these patient populations is anticipated to be especially effective.

Keywords: JAK/STAT signaling, cancer, STAT5, chromosomal locus

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The role of mesenchymal stem cells and Imatinib in the process of liver fibrosis healing through CCL2-CCR2 and CX3CL1-CX3CR1 axis (Research Paper)

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Introduction: Perpetuated damages of liver conduce to liver fibrosis, accompanied by the aggregation of extracellular matrix. Macrophages play a critical role in this phenomenon. The CCL2-CCR2 and CX3CR1-CX3CL1 axes are main regulators of macrophage calling, liver infiltration, and differentiation. Here, using a rat model of carbon tetrachloride (CCL4)-induced liver fibrosis, we sought to ascertain the effects of imatinib and bone marrow-derived mesenchymal stem cells (BM-MSCs) on the expression of these axis.

Methods: 16 Sprague-Dawley rats in four groups of healthy, liver fibrosis, imatinib-recipient, and BM-MSC-recipient were studied. Histopathology and Sirus-red were used to assess the treatment effects of planned techniques. For the purpose of identifying changes in the expression of the genes CCL2, CCR2, CX3CL1, and CX3CR1, quantitative real-time PCR was used.

Results: Histopathological findings showed the effect of imatinib and BM-MSCs in the amelioration of liver fibrosis. Our findings indicated that CCL2 and CCR2 expression had significantly diminished in imatinib and BM-MSCs therapies compared to the liver fibrosis group. Conversely, CX3CL1 and CX3CR1 gene expression showed an increase in both therapeutic groups than liver fibrosis groups.

Conclusion: The significant decrease in CCL2-CCR2 genes in both therapeutic groups suggests that BM-MSCs and imatinib might lead to a decline in inflammatory macrophages within the liver. The lower CCL2-CCR2 expression in imatinib-recipient showed the better performance in the modulation of inflammatory macrophage recruitment. The higher expression of CX3CL1 in BM-MSC-recipient showed the higher effect on and polarization of LY6Chigh (inflammatory) to LY6Clow (anti-inflammatory) macrophages, which tread a path for further investigation

Keywords: CCL2, CCR2, CX3CL1, CX3CR1, Liver fibrosis

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The Role of microRNAs and circularRNAs in diagnostic, Prognostic and therapy response as Personalized Oncology Biomarkers in prostate cancer (Review)

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Introduction: Small noncoding RNAs known as microRNAs (miRNAs) control protein expression at the post transcriptional level as well as Circular RNAs (circRNAs) are a unique family of noncoding RNAs that could regulate multiple biological processes, which play a crucial role in carcinogenesis, progression and chemotherapy resistance of cancers. These RNAs influence a wide range of biologic processes and are often deregulated in cancer .circRNAs and microRNAs play a key roles in the development of cancer and are therefore a potential marker for diagnosis, prognosis, and therapeutic choices in prostate cancer (PCa) patients. To review the currently available data on circRNAs and microRNAs as biomarkers in PCa and as possible tools for early detection and prognosis.

Methods: Review was performed searching the PubMed and ،Science direct ،Embase ،Cochran وScopus database for articles in English using the following terms: circularRNA, circRNA, microRNAs ,miRNAs ,cancer, prostate cancer, circRNA and miRNAs profiling, diagnosis, prognosis, therapy response, and predictive marker. We summarize the existing literature concerning the profiling of circRNA and microRNAs in PCa detection, prognosis, and response to therapy

Results: The circRNAs and miRNAs are important regulators of biologic processes in PCa progression. A common expression profile characterizing each tumor subtype and stage has been identified for Pca diagnosis,prognosis and therapy response,. Large-scale studies that should provide additional important information are still missing. Further studies, based on common clinical parameters and guidelines, are necessary to validate the translational potential of circRNAs and miRNAs in PCa clinical management.

Conclusion: The literature shows that circularRNAs and miRNAs hold potential as novel biomarkers that would aid prostate cancer management, but additional studies with larger patient cohorts and common guidelines are necessary before clinical implementation.

Keywords: prostate cancer, circular RNA, biomarker, micro RNA

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The role of miRNAs in bacterial infections (Review)

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Introduction: Pathogenic bacteria cause various infectious diseases worldwide, especially affecting people with weakened immune systems and susceptibility to other infectious diseases. MicroRNAs (miRNAs) are constrained non-coding RNAs that control gene expression at the post-transcriptional level. They are expressed by eukaryotic cells and play essential roles in shaping cell differentiation and organismal development. In addition to being involved in various physiological and pathological processes, including viral infections, microRNAs are increasingly involved in eukaryotic responses to bacterial pathogens. It is becoming increasingly clear that miRNAs are an essential part of host responses to microorganisms.

Methods: We used the words ‘MicroRNAs’, ‘ bacterial infections, and ‘ non-coding RNA ’ in the published data in PubMed, Scopus, and Google Scholar databases for this study.

Results: This study addresses our current understanding of the role of miRNAs in responding to bacterial pathogens.

Conclusion: The use of dysregulated miRNAs in bacterial infections may be an approach to improve the diagnosis, prevention, and treatment of infectious diseases.

Keywords: MicroRNAs, non-coding RNA, bacterial pathogens, immune systems

The role of miRNAs in proliferation of colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) is known as the third most common cancer as well as the fourth most deadly cancer worldwide. As Western diets and lifestyles have had an increasing impact on human health, a rise in CRC incidence rates has followed. The risk factors for CRC include environment, family history, age, obesity, smoking, alcohol, low physical activity, and poor nutrition. CRC accounts for approximately 10 % of all new cancer cases globally, remaining the second most frequent cause of cancer-related deaths. Identification of the influencing factors and molecular mechanisms in CRC progression and chemoradiotherapy plays a vital role in CRC treatment. MicroRNAs (miRNAs) are a class of small noncoding RNAs which can bind to target mRNA and induce downregulation of target protein through translation inhibition, mRNA cleavage or degradation. A single kind of miRNA can target hundreds of mRNAs, affecting the expression of many genes that are often involved in the pathway of functional interaction. This study's aim was to investigate the role of miRNAs in colorectal cancer.

Methods: this review investigating the role of miRNAs in the proliferation of colorectal cancer has been written from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Unrestricted proliferation of human CRC is the basis of cancer development in which miRNAs play a significant role. Various miRNAs target a variety of proliferation-related genes consisting of miR-143 and miR-145 (miR-143/145). Michael et al. first reported the association between the miR-143/145 cluster and CRC in 2003, and they revealed decreased expression of miR-143/145 in colorectal tissues compared to normal tissues. There is a consensus that miR-143/145 are tumor suppressor miRNAs. In CRC tissues, the downregulation of miR-143 increased the expression of DNMT3A. Upregulated DNMT3A promote CRC progression, which is associated with DNA methylation. Furthermore, Hu et al. demonstrated that PART1 competed with DNMT3A for binding miR-143, which meant that PART1 might also be a useful therapeutic target. miR-145, which is co-expressed in the same cluster with miR-143, was demonstrated to inhibit IGF1R with miR-143 and repress CRC proliferation. Moreover, it was reported that miR-145 served as an oncosuppressor, and CRC cells treated with miR-145 mimics showed a

decrease in their proliferation, which also indicated that miR-145 had a potential role in CRC treatment. Another important set of miRNAs, the miR-17~92 cluster, including miR-17, miR-18a, miR-19a, miR-19b-1, miR-20a, and miR-92a, is related to multiple cancers such as lung cancer, prostate cancer, and colorectal cancer. Investigators found that miR-17, miR-106a/b and miR-20a/b could target GABBR1 to regulate GABB signaling during CRC proliferation. miR-17 is the most upregulated member of the miR-17-92 cluster in the evolution of early colon cancer. Investigators reported that miR-17 promoted CRC proliferation by downregulating SIK1 expression. miR-20a and miR-106a have essential roles in CRC proliferation. Zhu et al. reported that upregulation of miR-20a and miR-106a caused the loss of AMER1 (also known as WTX), disrupting the interaction between RHOGDIα and CDC42, which resulted in accelerated CRC proliferation.

Conclusion: In conclusion, miRNA regulate multiple pathways of expression, such as the Hippo, Notch and Wnt/β-catenin signaling pathways, and the involvement of miRNAs plays a pivotal role in CRC proliferation. The Wnt/β-catenin signalling pathway is vital in CRC proliferation. It has been reported that approximately 90 % of CRC cases carry mutations in one of two genes in a typical Wnt/β-catenin signalling pathway, APC or CTNNB1, which has been confirmed in a recent large-scale sequencing project conducted by The Cancer Genome Atlas (TCGA). Mutations in APC or CTNNB1 usually lead to the accumulation of β-catenin, thus activating the Wnt/β-catenin pathway and promoting CRC progression.

Keywords: miRNAs, colorectal cancer, proliferation

the role of non-coding RNAs (LncRNA) in bladder cancer (Review)

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Introduction: Bladder cancer (BC) is one of the ten most common malignancies worldwide. Apoptosis, glycolysis and EMT are tightly regulated by long non-coding RNAs (lncRNAs) in the BC. LncRNAs are a group of RNA transcripts that do not encode proteins and are over 200 nucleotides in length. They play important roles in controlling cellular pathways and molecular interactions involved in the onset, development, and progression of various types of cancer. The response of BC cells to cisplatin, doxorubicin and gemcitabine chemotherapy is modulated by lncRNAs. LncRNAs regulate immune cell infiltration into the tumor microenvironment and affect BC cell response to immunotherapy. lncRNAs are able to regulate the pathways of microRNA, STAT3, Wnt, PTEN and PI3K/Akt and thus influence both proliferation and migration of BC cells. LncRNAs are potential biomarkers. Defective expression of lncRNAs in tumor cells is a hallmark of cancer, and lncRNAs can act as tumor suppressors or oncogenes depending on the cellular context and different functions of the target genes. This review investigates the role of LncRNA in bladder cancer.

Methods: For the subsequent systematic review, the necessary data were collected using the keywords and MeSH (medical title) terms listed below, where possible, and by reference to leading databases such as PubMed and Science Direct. Additionally, a manual search was performed using Google Scholar to increase the sensitivity of the search. The statistical study population includes all studies conducted in context between January 2018

and august 2023. After reviewing relevant results and evidence quality ratings, 12 English-language articles were reviewed.

Results: There are more than 100 dysregulated lncRNAs involved in the regulation of various BC biological functions such as cell proliferation, apoptosis and metastasis. 43 Increase in lncRNAs involved in BC proliferation, migration, invasion and cell cycle, such as UCA1, long noncoding RNA 19 (H19), taurine up-regulated gene 1 (TUG1), and Calmodulin Like 3 Antisense RNA 1 (CALML3-AS1). Cytoplasmic lncRNAs can work as oncogenes. UCA1, that overexpressed in bladder cancer, specifically induces Glutaminase 2 (GLS2) by sponging miR-16 and also can activate AKT by recruiting the E1A-binding protein P300 (EP300), which causes bladder cancer cells to grow. UCA1 can has another oncogenic function in bladder cancer by enhancing the mTOR/STAT3/HK2 signaling pathway that promotes the Warburg effect. and UCA1 is also modulated by upstream molecules such as bone morphogenetic protein 9 (BMP9), which then promotes the development of bladder cancer. lncRNA can be found in human biological fluids such as blood and urine. These lncRNAs are resistant to RNases, making them attractive as new non-invasive diagnostic and prognostic biomarkers. It is possible that urine is a better source of biomarkers for genitourinary diseases, including tumors. Common methods for analyzing the expression profile of lncRNAs are real-time polymerase chain reaction (real-time PCR), microarrays and next-generation sequencing (NGS).

Conclusion: vital functions of lncRNAs in BC, including: 1) growth regulation, cell cycle, glycolysis and apoptosis factors; 2) regulation of BC cell migration by influencing the EMT mechanism; 3) affect the treatment response and modulate the cytotoxicity of CP, DOX and gemcitabine towards BC cells, 4) regulate the immunosuppressive role of the TME and influence immune cell infiltration; 5) regulation of molecular pathways; and finally 6) considered diagnostic and prognostic. Since BC patients have a poor survival rate, the targeted use of lncRNAs can be considered an important tool to improve their prognosis Circulating lncRNAs can be enriched in urine supernatant and bladder cancer plasma, which could be useful in new bladder cancer tests. The aberrant expression of 36 lncRNAs has been suggested to be closely related to many clinical features of bladder cancer. Given the low and evolutionarily less conserved expression, increased lncRNAs represent advantageous features that may serve as diagnostic or prognostic markers for BC.

Keywords: long non-coding RNA, LncRNA, urinary bladder neoplasms, bladder cancer, neoplasms therapeutics

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The role of snp genes related to Alzheimer's disease as biomarkers in the early diagnosis of this disease (Review)

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1.

Introduction: In this article, we want to prevent the occurrence of Alzheimer's by knowing the SNPs of genes related to Alzheimer's ،Alzheimer's disease (AD), an extremely common neurodegenerative disorder of the older generation, is one of the leading causes of death globally.The etiology of Alzheimer's is complex, with numerous environmental and genetic factors contributing to the disease.Genome-wide single nucleotide polymorphism (SNP) data are now quickly and inexpensively acquired ،Alzheimer's disease is a neurodegenerative disorder with a slow onset and slow progression that occurs in middle age, so by knowing the snp genes of this disease, it is better to start treatment from a young age to prevent its occurrence. Finally, we offer some recommendations in areas where the field can rapidly advance towards precision interventions that leverage the ideas of protection and resilience for the development of novel therapeutic strategies

Methods: literature review

Results: There is no definitive treatment for Alzheimer's disease yet, so we must find a way to prevent its occurrence at a young age, one of which is the recognition of SNPs.

Conclusion: The correlation between genetic and functionality data may have an impact on several aspects of disease presentation and therapy, helping in prediction pattern of AD presentation and treatment efficacy. As a consequence it may lead to better patients quality of life and longer periods of self- sufficiency

Keywords: Alzheimer's disease, genetic polymorphisms (SNPs). Early diagnosis of the disease ABCA7, APOE, TRE

The Role of Stem Cells in Cancer Progression and Therapy (Review)

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Introduction: Primary cancer cells have been found to derive from stem cells, with a subsection of these cells named “cancer stem cells” (CSC’s). CSCs replicate similar characteristics to regular stem cells, such as the ability to proliferate in their microenvironments. CSCs sustain cancer by promoting proliferation and therefore must be targeted when attempting to eliminate cancer for successful and long-lasting results. As do most healthy cells. This study's objective was The Role of Stem Cells in Cancer Progression and Therapy.

Methods: This review study has written the Role of Stem Cells in Cancer Progression and Therapy from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The results show performed simultaneous silencing of CD-47 and PD-L1 in order to enhance immunotherapy against circulating tumor cells. Inhibiting PD-L1 allowed immune cells to locate tumor cells more adequately, and blockade of CD-47 permitted macrophage-mediated destruction of the tumor cells. In vitro flow, cytometry confirmed overexpression of CD-47 and PD-L1 in the tumor cell line.19 Compared to the blank controls or single-antibody group, dual inhibition of these immunosuppressive proteins resulted in a more potent reduction of solid tumors in mice. In order to target CD-47 and silence its downstream effects, various forms of pharmacological and nanomedicine-based approaches have been established. An antibody named Hu5F9-G4 that targets CD-47, allowing macrophages to destroy the cancer cells, has been developed. Another similar antibody, Rituximab, which has been known to amplify destruction signals inhibited by CD-47 positively, is highly active and is well tolerated as first-line single-agent therapy for indolent non-Hodgkin lymphoma (NHL). Using the application of both antibodies, Hu5F9-G4 and Rituximab, the results of a clinically evaluated study on the treatment outcome in patients of NHL concluded that at least 50% of the test subjects had eliminated most symptoms of cancer.

Conclusion: Silencing cell surface markers on CSCs can promote immune recognition of tumor sites and inhibit the binding of tumor cargo to healthy cells, thus preventing their transformation. immunotherapy towards many forms of cancer by targeting cancer stem cells. This is because, in the past,

various CSCs in cancers such as pancreatic, lung, and breast cancers have been proven to express CD-47. Hence, targeting this immune blockade molecule expressed in CSCs may provide a new avenue of cancer treatment.

Keywords: Stem Cells, Nanomaterials, Cancer Therapy

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The role of wild-type P53 in cancer (Review)

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Introduction: p53 protein or guardian of genome is the most famous tumor inhibitor of classic type. since more than 50% of human cancers are due to loss of function within p53 due to mutations. this protein has vital role in genomic stability and Tumor suppression through the induction of apoptosis and seizure of the cell cycle ,aging , inhibitor of angiogenesis.

Methods: in this review article tried to use data's of google scholar, pubmed, nih to conserned about p53 gene role in treatment of cancers.

Results: it is now known distruption of p53 mechanisms by affecting and paying attention to carcinogenic mutations causes growth and Tumors progression. The p53 mutation acts as dominant inhibitor compared to wild type of p53.Wild type of p53 (wt)protein can inhibit oncogen_induced cellular transformation.

Conclusion: in the current review article p53 regulatory mechanism and also p53 mediated therapeutic strategies for the treatment of malignant cancers are one of the expected factors, for chemotherapy providing a new strategy is for eliminating the negative effect of .p53 mutation within the(wt)

Keywords: therapeutic carcinogenic inhibitor

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The use of artificial intelligence in cell therapy for diabetic foot ulcers (Review)

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Introduction: Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia and is caused by a defect in the secretion or use of insulin or defective insulin activity. According to the statistics of the World-Health-Organization, about 422 million people worldwide have diabetes. Diabetic foot ulcers (DFUs) are one of the most common complications of diabetes mellitus. (About 19-34% of diabetic patients suffer from DFUs during their lifetime.) DFU describes a break in the skin of the foot in a person with diabetes that does not heal quickly. The ability to self-renew and differentiate into various types of cells are the main characteristics of stem cells, which make cell therapy a new alternative for tissue repair and regeneration. The possibility of using mesenchymal stem cells (MSCs) as a cell source for tissue engineering applications including bone regeneration, cartilage regeneration, and DFU has been shown based on the role of these cells in wound healing. In recent decades, new therapeutic methods based on MSCs have been designed to solve the medical problems of patients with incurable DFU. Although cell therapy seems simple in theory, due to the non-homogeneous nature of cells, existing test methods may have more errors than expected. Scientists believe that artificial-intelligence (AI) can help provide precise measurements to solve this complexity, which could be a big step in cell-therapy for chronic diseases such as DFU. In short, AI is the science of building intelligent machines that can imitate human behavior using learning and decision-making abilities with minimal external intervention. Considering the fact that there has been no study on the use of AI in the cell therapy of this chronic complication of diabetes, the purpose of this review article is to propose the use of AI in the cell therapy of diabetic foot ulcers.

Methods: For this study, using PubMed, Medline, ScienceDirect, and Web of Science search engines, we studied articles related to the use of AI in cell therapy and cell therapy for diabetic foot ulcers.

Results: AI can analyze large data sets in a short time and lead to improved patient treatment. By implementing AI algorithms, researchers can find cells that are most likely to grow, proliferate, and differentiate in target tissues. Researchers are using artificial-intelligence in cell therapy to predict the

therapeutic potential of cells to develop patient-specific regenerative therapies. Also, artificial-intelligence is vital for improving the quality of production and delivery of stem cells and can help in determining the viability, effectiveness, efficiency, and safety of stem cells. Using methods such as patient classification based on machine learning to identify patients who respond to treatment or not before treatment with stem cells, which can reduce treatment costs, is one of the effects of this science in cell therapy. A paper published in 2021 stated that advanced AI algorithms should be used to manage large volumes of medical data sets that include individual genetic characteristics, clinical findings, laboratory biomarkers, and computational analyses in stem cell therapy. For example, in a 2020 study on cell therapy for age-related macular degeneration, artificial-intelligence was used to predict tissue function based on the shape characteristics of individual donor cells, with only one error out of 36 predictions. which shows that this non-invasive method can minimize errors and prevent adverse effects in the field of cell-therapy.

Conclusion: In recent years, artificial-intelligence-based technologies have been developed to improve remote monitoring of diabetic foot ulcers using mobile phone applications. Aspects such as timely screening to identify the risk of leg ulcers (or even worse, amputation) have also been addressed through this science. It has been shown that AI can use real-world data to create models capable of predicting and medically diagnosing diabetes and its complications, such as diabetic foot ulcers. However, despite the large number of diabetic patients who are involved in DFU, as well as the importance of stem cells in the treatment and control of these patients and the prominent role of AI in tuberculosis therapy, no study has been conducted on this issue. Emphasizing the importance of using AI in cell-therapy and also using cell-therapy in the treatment process of diabetic foot ulcers, this review article suggests the use of artificial-intelligence in the treatment of diabetic foot ulcers.

Keywords: diabetic foot ulcer, cell therapy, artificial-intelligence

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The Use of Magnetic Nanoparticles for Sample Preparation of Biomarkers Related to Human Diseases (Review)

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Introduction: Measuring clinically important biomarkers is critical for understanding disease progression and conducting clinical trials. However, the complexity of biological fluids makes analyzing trace biomarkers challenging. Magnetic solid phase extraction has recently emerged as a promising approach for sample preparation due to its magnetic separation, versatile surface chemistry, and environmental friendliness.

Methods: This review summarizes recent advances in using magnetic materials for biomarker extraction and analysis in clinical applications. It aims to highlight the potential of magnetic solid phase extraction to improve sensitivity and selectivity for biomarker detection.

Results: Relevant literature on magnetic materials for clinical biomarker sample preparation and analysis was systematically reviewed. Key findings on synthesis strategies, surface modifications, and applications were summarized. Recent studies demonstrate magnetic extraction can selectively isolate biomarkers from complex clinical samples like plasma, serum, and urine. Magnetic nanomaterials with tailored surface chemistry allowed clinically relevant limits of detection. Examples include cancer biomarkers, neurotransmitters, and pharmaceuticals.

Conclusion: Magnetic solid phase extraction shows significant promise for improving clinical biomarker analysis. Continued research on novel magnetic materials and surface modifications is warranted. This review provides insights for those aiming to develop magnetic extraction protocols for sensitive, selective clinical diagnostics.

Keywords: Biomarkers, Magnetic nanoparticles, Sample preparation, Clinical diagnostics, Magnetic solid phase e

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The use of nanocurcumin based on chitosan in cancer treatment (Review)

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Introduction: In recent decades, natural polymers, especially polysaccharides, have been used as carriers to deliver a wide range of therapeutic agents. Chitosan, the second most abundant natural polysaccharide after cellulose, is a biocompatible, biodegradable, hydrophilic, non-toxic, high bioavailability polymer, capable of forming films, gels, nanoparticles, microparticles, and granules. Curcumin is a yellow polyphenol extracted primarily from the Curcuma longa plant, but also from several other members of the ginger family. To overcome the aqueous solubility and poor bioavailability of the drug curcumin, emphasize its functional properties, and expand its applications in the pharmaceutical industry, many nanoscale systems have been widely used for drug loading and release. Over several decades, chitosan has been widely used as a natural biopolymer. It was studied due to its polycationic nature, biodegradability, biocompatibility, non-toxicity and non-allergenicity. The present study is a review of the findings of the use of nanocurcumin based on chitosan in cancer treatment.

Methods: In this study, by searching Pubmed, Cochrane, Web of Science, Google Scholar and Scopus databases, relevant studies were searched from the beginning to 2023 and the resulting studies were reviewed.

Results: Chitosan is a linear polysaccharide obtained by deacetylation of chitin. Also, biodegradable chitosan breaks down in the human body into safe compounds (amino sugars) that are easily absorbed. Chitosan has hydroxyl and amine functional groups that can be modified to achieve specific goals, turning it into a polymer with a wide range of potential applications. The findings show that research on chitosan-based systems containing various drugs, including curcumin, for various therapeutic applications such as cancer treatment has increased in recent years. The results of various studies showed that the use of formulated curcumin, on the one hand, increases its absorption and bioavailability, and on the other hand, increases its effectiveness on cancer cells, including breast cancer, and these results can indicate the beneficial effects of curcumin nanoformula compounds in Prevention and treatment of breast cancer.

Conclusion: The development of colloidal systems for the encapsulation of curcumin release is a promising strategy to overcome the limitations of drug release. In this research, chitosan-based nanocarriers and their physical and chemical properties, such as surface charge, morphology, encapsulation driving force, and release characteristics, have been investigated. These characteristics determine the performance of chitosan-based nanocarriers for pharmaceutical applications. Due to the higher bioavailability of formulated compounds of curcumin compared to the free form of curcumin and due to the low toxicity of this herbal medicine, it can be used along with other anticancer drugs in the treatment of breast cancer.

Keywords: nanocurcumin, nanomedicine, nanotechnology, cancer

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The use of stem cells for the cornea of the eye by natural lenses (Review)

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1. Shahed Reyhana Al-Nabi

Introduction: Treatment with limbus transplantation has been developed for superficial eye diseases and damage that causes limbus stem cell defects, and eye epithelial stem cells can improve the surface and internal function of the eye as well as the cornea with natural lenses.

Methods: Epithelial cell and stem cell culture method was used by heat shock proteins and after culture, the cells should be prepared from the separated culture medium for transplantation and in fact amniotic membrane with extracellular matrix elements such as fibronectin-laminin-collagen IV and growth factors EGF, bFGF, HGF are effective in maintaining stemness properties in limbal epithelium stem cells. And it was transplanted with a natural lens on the cornea of the patient's eye. If both stem cell transplants of the limbus area and cornea transplant were needed, these operations were performed simultaneously or sequentially.

Results: The results of this test indicate that when the epithelial cells were cultured in the processed medium and transplanted with the cornea by a natural lens, the internal inflammations were reduced and the patient was able to get rid of his annoying eye diseases.

Conclusion: Dental pulp stem cells, hair follicles, and bone marrow mesenchymal cells are among the investigated sources, and in animal models, the possibility of using these cells and their ability to form corneal epithelial cells has been confirmed, and by conducting additional tests and confirming the results In human models, they will probably replace today's common methods in the near future.

Keywords: Stem cells, eye cornea, morphology, limbal, epithelial

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The use of stem cells in the treatment of schizophrenia (Review)

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Introduction: Schizophrenia is a severe mental illness that has symptoms including hallucinations (often auditory hallucinations), thought disorder, social withdrawal, decreased motivation, decreased concentration, anxiety, decreased expression of emotions, indifference, etc. The symptoms of this disease usually start in early adolescence, and in many cases, they never go away completely. Reduced hippocampal volume, lack of hippocampal interneurons, functional and biochemical abnormalities in that area, as well as damage in the prefrontal cortex have been identified in the MRI study of schizophrenia patients. In healthy people, the prefrontal cortex of the brain regulates the release of a neurotransmitter called dopamine, while in patients with schizophrenia, the process of dopamine regulation by the prefrontal cortex is disrupted. So far, no definitive treatment has been found for schizophrenia, and most of these patients suffer from its complications for the rest of their lives.

Methods: Stem cells are a group of cells that are not specialized and become specialized cells with specific actions and activities under specific environmental or laboratory conditions. Recently, researchers are studying to treat schizophrenia with the help of stem cells. Stem cells taken from the embryos of mice and injected into the hippocampus of mice with schizophrenia, improved the brain functions in these mice. Current methods for treating schizophrenia are drug treatments that are temporary at best, but stem cells injected into the hippocampus of schizophrenic mice have improved schizophrenia symptoms and improved brain functions.

Results: Stem cells injected into the hippocampus and prefrontal cortex of schizophrenic mice became interneurons that regulate dopamine release and improved the function of the prefrontal cortex and hippocampus in these animals. In these mice, complications such as memory impairment, social withdrawal, reduced motivation and reduced concentration caused by schizophrenia were improved. Although complete studies have not been conducted on the possible long-term side effects of stem cell injection, such as immune response to stem cells, infection, increased brain pressure, etc., the results obtained so far have raised hopes for the clinical treatment of schizophrenia with the help of stem cells.

Conclusion: The studies that have been conducted so far on the treatment of schizophrenia with the help of stem cells show that the stem cells of the bone marrow, fat tissue, and umbilical cord, when injected into the hippocampus of mice with schizophrenia, turned into interneurons that regulate the release of dopamine, and improved the effects caused by chizophrenic.

Keywords: Schizophrenia; Stem cells; Hippocampus; Prefrontal cortex

Therapeutic applications of Platelet-rich plasma (PRP) in women's health and infertility: A Review Article (Review)

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Introduction: Platelet-rich plasma (PRP) is a new treatment method that which is enriched with large amounts of platelets and growth factors. Growth factors play an essential role in tissue regeneration and activate cell growth and reproduction and in this way, it is used in various skeletal-muscular diseases. PRP plays an important role in problems related to women's health and infertility, that have remained a major troublesome clinical problem, despite various treatments. In this article, we reviewed the therapeutic different uses of PRP in the field of women's health.

Methods: At ISI -Scopus-Pub med-Medline- Google Scholar databases, we examined 31 studies conducted in the years 1978-2023 regarding the usage of PRP in women's health and infertility.

Results: PRP is as a growing and robust therapeutic option in medicine that although the efficacy of PRP as a treatment method has not yet been definitively proven, and the United States Food and Drug Administration (FDA) has not approved PRP injection as a treatment method, but many cases of recovery have been seen in different patients. PRP can solve problems related to women's health and infertility in two ways: PRP of ovaries and uterus. PRP injection into the ovary is used to rejuvenate the ovary and improve its function in various cases including: treatment of premature ovarian failure syndrome and improvement of ovarian reserves in order to restoring fertility in women with early menopause or women with low ovarian reserve or infertile due to hormonal problems. Uterine PRP can stimulate the production of new tissue in the uterus with its growth factors. Then it increases the endometrial thickness and improves pregnancy outcomes in various cases including: Increase the chances of fertility success in in women that are suffering from unexplained recurrent implantation failures (RIFs) and repeated pregnancy loss (RPL) undergoing in vitro fertilization (IVF) treatments, treatment and increase fertility in patients with hypoplasia endometrial (especially in cases where the endometrium does not grow with medication), chronic endometritis, endometriosis and Asherman syndrome, also improvement of complications after surgery and after abortion. In patients with a history of RIF-RPL in IVF cycles , PRP is usually performed 36-48 hours

before embryo transfer. It is important to note that failure of infertility treatment methods depends on several factors such as chromosomal disorders, embryo transfer technique, uterine problems, etc.; So, as a rule, using only one treatment method cannot solve this problem and significantly increase the chances of fertility success. Research shows that the use of uterine PRP only affects the uterine endometrium. Another advantage of PRP is that no synthetic material is used and it does not cause immune system reactions against the injected material. In addition, it has a short recovery period and is not invasive.

Conclusion: Platelet-rich plasma (PRP) can be a promising therapeutic solution in women with women with uterine and ovarian problems and become the basis for increasing the chance of reproductive success in them.

Keywords: Platelet-rich plasma (PRP) - women – Infertility

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Therapeutic cell-based vaccines for glioblastoma multiforme (GBM) (Review)

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Introduction: Glioblastoma multiforme (GBM) is one of the deadliest types of tumors. Conventional treatments available are surgery, radiotherapy, and chemotherapy. However, the overall survival rate of patients is extremely low, mainly due to significant drug delivery challenges and tumor heterogeneity. Therefore, novel effective treatments are urgently required, among which cancer vaccines represent a promising candidate. In the current study, we will review therapeutic vaccines used for GBM treatment, with a focus on cell-based vaccines including dendritic cell (DC) and tumor cell vaccines.

Methods: In this review, we summarized the information from 45 clinical trials in which cell-based vaccines have been used for the treatment of GBM in more than 1500 patients, and further data were collected using PubMed, Web of Science, and Google Scholar databases.

Results: These vaccines have not been associated with significant toxicity and have been reported to be safe. Based on the findings of these clinical studies, the use of cell-based vaccines can slightly increase overall survival and progression-free survival in patients. However, this therapeutic modality is faced with several limitations including the insufficiency of antigenic activity of GBM to boost immune response and dose optimization.

Conclusion: To make cell-based vaccines the preferred standard treatment for GBM, more investigations are required to address their current limitations.

Keywords: Glioblastoma; vaccine Dendritic cells; Tumor cell vaccine; Immunotherapy

Therapeutic effects of D aspartate in a mouse model of multiple sclerosis (Research Paper)

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Introduction: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) that leads to an inflammatory demyelination and axonal damage. Experimental autoimmune encephalomyelitis (EAE) is experimental animal model for the study of MS. The purpose of the present investigation was to assay the therapeutic efficacy of D aspartic acid (D Asp) on a mouse EAE model.

Methods: Myelin 40 oligodendrocyte glycoprotein (35 55) in a complete Freund s adjuvant emulsion was used to induce EAE in female C57BL 6 mice, and D Asp was operated to test its efficiency in the reduction of EAE. Throughout the study period, clinical evaluation was assessed. On 21st day after induction EAE, blood samples were taken from the right ventricle of the heart for the evaluation of interleukin 6 and other chemical molecules. The mice were sacrificed, and their brain and cerebellum were removed for histological analysis.

Results: Our findings illustrated that D Asp had beneficial effects on EAE by reduction in the severity and delay in the onset of the disease. Histological analysis displayed that treatment with D Asp can decrease inflammation. In addition, in D Asp treated mice, the serum level of interleukin 6 was significantly lower than that in control animals, whereas the total antioxidant capacity was significantly higher.

Conclusion: The data represents that D Asp possess neuroprotective property, so it is able to prevent the onset of the multiple sclerosis.

Keywords: Experimental autoimmune encephalomyelitis, Multiple sclerosis, Antioxidant, D aspartic acid, D aspa

Therapeutic impact of Ozone administration on Breast cancer treatment: a comprehensive review (Review)

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Introduction: Breast cancer as a highly heterogeneous disease increases the death rate worldwide over time. For the last decade, studies have shown that ozone therapy has an anti-proliferative effect on cancer cells without affecting non-cancerous cells. The mechanism is to increase the blood oxygen level, reducing tumor hypoxemia. Accordingly, researchers extended investigations in in-vitro, in-vivo, animal models, and clinical studies of solid tumors, including breast cancer.

Methods: Herein we considered assessing ozone therapy's overall impact in recent contributed literature on cancer with specific insights on breast cancer.

Results: Many studies provided evidence of ozone therapy's immunomodulatory impact and sensitizing effect on chemotherapy and radiotherapy. Also, ozone therapy seems to help fatigue relief in cancer patients and cancer resection healing. Although the FDA did not provide any agreement to ozone administration in cancer patients, it elucidated that ozone is a harmful and toxic air pollutant. By that intravenous administration of ozone resulted in pulmonary embolism and death, it is critical to assess if the recent investigations prove the security and efficacy of therapeutic ozone in cancer. Besides, ozone accurate delivery is crucial. Nowadays ozone is considered a complementary treatment in many conditions at the clinical level and some administration approaches in the hands of specialists achieved their safety and efficacy profile.

Conclusion: In conclusion, ozone therapy in breast cancer profile suffers from a lack of investigations and clinical studies. Many reviewed literature have claimed that ozone is safe and effective in case of breast cancer treatment, even as integrative therapy or palliative therapy to increase the quality of life. However, it is essential to conduct more investigations and more clinical experiments to conduct systematic reviews of randomized controlled trials (RCT) studies.

Keywords: Keywords: Ozone-therapy, Breast-cancer, Immunomodulatory, Radio-sensitizer, Chemo-sensitizer

Therapeutic potentials of regenerative medicine and tissue engineering in the field of orthopedics (Review)

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Introduction: The goal of orthopaedic joint therapies is to restore pain-free function with minimally invasive procedures. Stem cells have the potential to revitalise damaged ligaments, cartilage and bone. However, regenerative medicine has not yet achieved clinical acceptance in orthopaedics. Stem cells have the potential to revolutionize orthopaedic practice, and this article aims to provide a complete overview of the clinical advances in this field. Stem cells can be obtained from various sources, but bone marrow, adipose tissue and muscle-derived MSCs are most commonly used. Mesenchymal stem cells (MSCs) have the potential to develop into any mesodermal tissue, including bone. Biologic augmentation can help heal nonunion/delayed union and bone defects following trauma, tumor or infection. Autologous cancellous graft is the "gold standard," but limited supply and donor site morbidity limit their use. Allografts and bone graft substitutes are routinely used, but poor graft integration and osteonecrosis of the graft remain primary issues. Bone marrow aspirates have been successfully used to enhance healing of non-unions.

Methods: In order to review the studies of regenerative medicine and tissue engineering in the field of orthopedics, articles with keywords regenerative medicine, tissue engineering, orthopedics, stem cell, platelet-rich plasma, stem cell isolation methods, types of stem cells, growth factors, scaffold in Time period from 2010 to 2023 in the database Pubmed and google scholar reviewed.

Results: Stem cells can be administered through various routes, and they have the ability to differentiate and secrete growth factors and cytokines that play a role in angiogenesis, repair, cell survival and proliferation. Genetically modified MSCs are being developed for long-term release of growth factors. Tissue engineering with stem cells and scaffolds have been found to be useful

for bridging bone defects. MSCs alone have not proven to be beneficial for filling defects caused by simple/aneurysmal bone cysts, but healing rates are enhanced when used with scaffolds such as HA, DBM and TCP. Currently, among the new treatment methods for osteoarthritis and tendonopathy diseases, using the reconstructive medicine method, including injection: ¬ Platelet-rich plasma. ¬ Mesenchymal stem cells: stem cells obtained from adipose tissue, bone marrow, and pregnancy-associated sources like the umbilical cord, amniotic fluid, and the placenta. ¬ Biomaterials - organic substances such as autologous chondrocytes (cells procured from the patient that generate cartilage), bovine collagen, bone matrix, and proteins. Regenerative medicine techniques, specifically orthobiologic injections, provide solutions for clinical issues like tendinopathies and degenerative arthritis that have previously shown limited response to medication, rehabilitation, surgery, or joint replacement surgery, with biological therapies emerging as promising treatment options for musculoskeletal disorders in young adults and the elderly. Regenerative Medicine and Tissue Engineering (TE) have raised the hopes and expectations in medicine and created the hope of repairing or replacing the human tissues damaged by disease or trauma.

Conclusion: Regenerative medicine and biological methods are recognized as the next-generation advances in treating musculoskeletal conditions. Exciting options include autologous blood derivatives, cytokines, and cell-based therapy. Biological therapies using PRP and BMC are commonly used in orthobiology for various clinical problems such as osteoarthritis, tendon repair, chondral lesions, and soft tissue repair. Additionally, there is potential for treating nerve conditions and injuries. Cell therapy appears to have the most potential for tissue healing and regeneration. Musculoskeletal tissues like cartilage and ligaments do not heal well due to poor vascularity. Regenerating these tissues requires cells, morphogenetic signals, scaffolds, and a suitable mechanical environment. Treatment strategies could involve stimulating healing response, genetic alteration, cellular signaling changes, and exogenous augmentation with scaffolds. Regenerative medicine offers the potential to postpone and potentially minimize the need for surgical procedures in individuals experiencing degenerative joint ailments and musculoskeletal traumas. In the imminent future, there is a possibility that orthobiologics could be employed as an intermediate approach for ailments like arthritis, occupying a position that lies between conservative treatments (such as steroid injections) and surgical intervention.

Keywords: Regenerative medicine , Stem cell, Orthopedics , tissue engineering, Biological therapies

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Title : Insighte to brucella bacteria and other diseases between human and animals (Review)

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Introduction: Introduction: Brusellosis is a common disease between humans and animals which is caused by brucella bacteria .this is a common diseases between humans and animals. The highest rate of human brucellosis has been recorded in the MiddleEast and Central Asia Brucellosis is caused by bacteria of the genus Beucella Which is an Facultative intracellular gram-negative coccobacillus They are non-sporulating and non-encapsulated and there are reservoirs in it and it can infect soft tissues and organs.

Methods: Material Method: Tetracycline and doxycycline are combined with other drugs. The analysis related to brucellosis was collected from 2010 to2020 and the studies in the case werw economic effects and antibiotics and molecular epidemiology studies. Examination for 2 people “one was 29 years old and other was 45 years old. The HIV results were negative for both. The spine had epidural inflammation the result of blood culture before antibotice administration were negative after 5 days.

Results: Results: Bacterial genomic DNA was investigated and genome sequencing and analysis was performed both bacterial isolates are gram-negative and non –hemolytic. Both showed a positive reaction for cytochrome oxidase catalase and a negative result for indole. Diagnostic methods (molecular culture) performed on several patients to provide the best. Among the methods that have these advantages is polymerase chain reactin . Materials and ways : Blood samples were taken from 100 suspectedbrucellosis pationts with symptoms . The samples wereinoculated in 5%at 37 degrees for 21 to 31 days. After genome extraction `it was done according to the protocol. Out of 100 samples “ 2 samples were positive

Conclusion: Conclusion : Increase the necessary measures to control the infection and reduce the diseases. Not all cases can be detected `and in some cases`positive samples are mistakenly detected as negative. Research has shown that this disease is seasonal and occurs mostly in late spring and early summer.

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Keywords: Brucellosis Epidemiology Bacterial

Title: Gonorrhea disease review article (Review)

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Introduction: Introduction: gonorrhea is the second most common sexually transmitted infection of bacterial origin . the disease was initially described approximately 3,500 years ago, but it was not until 1879 that Albert Neisser determined the etiologic agent of the disease. Neisseria gonorrhoeae (the gonococcus) is a Gram-negative diplococcus and an obligate human pathogen .Gonococcal infection usually results from the transmission of N. gonorrhoeae through sexual contact. The pathogenetic hallmark of gonococcal infection is a host innate immune-driven inflammatory response, characterized by a potent neutrophil influx. In females, gonococcal cervicitis may lead to pelvic inflammatory disease, which may be antecedent to ectopic pregnancy and infertility even among those who are asymptomatic. Infection during pregnancy may cause miscarriage or premature birth and gonococcal conjunctivitis of the newborn. In males, infection may result in urethritis and epididymo-orchitis.If left untreated, gonorrhea in rare cases may cause bacteremia and disseminated infection.For these reasons, mitigating its spread is of critical public health importance. In addition, resistance to some antibiotics, such as azithromycin, is also increasing among gonorrhea cases whereas dual therapy with ceftriaxone and ceftriaxone plus azithromycin has also seen confirmed treatment failures.

Methods: Material methods: In 2020 the Centers for Disease Control and Prevention (CDC) reported that there were 333,004 new cases of gonorrhea in the United States, with an incidence of 106.1 cases per 100,000 population Worldwide, 106.1 million people are infected by N. gonorrhoeae annually.Currently, a more worrying trend has emerged, in that, there now appears to be an increased risk for HIV infection in patients that are also infected with N. gonorrhoeae. pathogeni factors of N. gonorrhoeae possesses a wide range of virulence determinants, which include the elaboration of pili, Opa protein expression, lipooligosaccharide expression (LOS), Por protein expression and IgA1 protease production that facilitates adaptation within the host .

Results: Results: However, a problem exists in the development of any vaccine in that antibodies within normal human serum bind to the gonococcal

outer membrane protein Rmp with binding apparently, having important consequences with regard to serum resistance for the organism . The presence of cross-reactive Rmp antibodies also facilitates transmission and women with Rmp antibody titers appear at an increased risk for infection .

Conclusion: Conclusion: In 2020 the Centers for Disease Control and Prevention (CDC) reported that there were 333,004 new cases of gonorrhea in the United States, with an incidence of 106.1 cases per 100,000 population Worldwide, 106.1 million people are infected by N. gonorrhoeae annually.Currently, a more worrying trend has emerged, in that, there now appears to be an increased risk for HIV infection in patients that are also infected with N. gonorrhoeae.

Keywords: sexually transmitted _pelvic inflammatory _ urethritis _ ceftriaxone plus azithromycin _vaccine

Title: Insight to Monkey pox disease , treatment and vaccination (Review)

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Introduction: Introduction: Monkey pox is a common disease between humans and animals. Monkeypox virus was first isolated in late 1985 from a colony of cynomolgus monkeys. Between 1960 and 1968, several other outbreaks were reported in monkey colonies in the United States and the Netherlands, but no human cases were observed during these outbreaks. The first case of this disease in humans was found in 1970. This case occurred in a 9-month-old boy who started with fever and developed a centrifugal rash after 2 days. The patient presented with otitis, mastoiditis and painful lymph nodes in the neck, and monkey pox virus was isolated from his skin lesions.

Methods: Material methods: He recovered from monkeypox, but before discharge developed measles, which resulted in his death. In 2003, the first cases outside of Africa were reported. These cases occurred in the United States and were associated with the importation of Gambian possums from Ghana into Texas In 2018, five infected patients were identified: three in the UK, one in Israel and one in Singapore. These cases were related to the arrival of people from Nigeria. Monkey pox virus belongs to family Poxviridae, subfamily Chordopoxvirinae and genus orthopoxvirus. This genus includes many other poxviruses, including poxviruses, vaccinia, cowpox, and camelpox, as well as recently isolated poxviruses. These double-stranded DNA viruses are genetically and antigenically very similar, which confers cross-immunity. Lesions often occur on the palms and soles, a feature that distinguishes monkeypox from chickenpox.

Results: Results: This disease is more severe in children and pregnant women. Monkeypox usually follows a self-limiting course, but clinical sequelae, including pitting facial scars, are common.

Conclusion: Conclusion: All lesions are usually in the same stage of development, another characteristic that distinguishes monkeypox from other diseases with skin manifestations such as chickenpox. Patients are often

itchy. The severity of the symptoms and the duration of the disease are proportional to the density of the skin lesions.

Keywords: Key words: Monkey pox Virus Follow up Clinical

Transcriptome analysis of a scorpion venom gland revealed the presence of a beta-toxin, a potent bioinsecticide. (Research Paper)

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Introduction: Scorpion venom is a valuable source containing various potent biomolecules. Over the years, the unique physiological properties and biochemical characteristics of scorpion peptides have been discovered by researchers. They represent novel potent compounds for development of novel drugs. More studies illustrate the pharmacological effect of venom components and their importance in treatment of diseases, including cancer, cardiovascular, microbial, autoimmune diseases and etc. Furthermore, Scorpion venom contains A2 phospholipases, serine proteases, metalloproteases, lipolysis-activating peptides (LVPs) and hyaluronidases, proteins and peptides (antimicrobial and toxic peptides that affect ion channels). Mesobuthus eupeus, a member of Buthidae family, is the most frequent scorpion species in Iran. This species is responsible for approximately 45% of scorpion sting cases in Iran. Small ion channel blocker peptides in scorpion venom cause various physiological effects in humans and insects, for instance: changes in the excitability of the central and peripheral nervous system, changes in the activity of smooth and skeletal muscles, and disruption of membrane stability by affecting ion channels. Therefor, identifying scorpion venom components uncovers important macromolecules responsible for scorpion sting symptoms or promising components for drug design or bioinsecticides.

Methods: After analyzing the transcriptome obtained using RNA extraction and subsequent cDNA library synthesis of the venom gland of Mesobuthus eupeus, blast analysis of obtained peptides was done. We found a novel beta-toxin affecting sodium channels, which represents unique potentials. Analyzing the structure and physiochemical characteristics of the recognized

peptide was done using Bioinformatic websites and software. Finally, three-dimensional structure of this peptide was determined by homology modeling.

Results: The newly recognized peptide consists of 73 amino acids containing eight cysteine residues forming four disulfide bridges, reveals a good solubility in water, theorical pI of 7.89 and molecular weight of 8336.53 g/mol. It was submitted to GenBank under the name meuNa8. meuNa8, shares a high similarity with a beta-insect excitatory toxin LqhIT1b from Leiurus quinquestriatus hebraeus. It is a potent anti-insect peptide.

Conclusion: meuNa8 is a potent small toxin-derived molecule, highly similar to the LqhIT1b, indicates the potential of affecting on the sodium channels of insects. Investigating the function of this protein in the future and identifying physiological processes will provide a lucrative hotbed for designing and production of safe biological insecticides.

Keywords: sodium channel blockers, biological insecticides, bioinsecticide

Transcriptomic evidence reveals anticancer effects of xanthohumol in a homospheroid model of cancer cells (Research Paper)

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Introduction: Humulus lupulus is one of the native plants of Iran that grows in the Northern provinces. Xanthohumol (XN) is the most important bioactive compound of Humulus lupulus, which has many uses in medicine. In this study, for the first time, the effect of XN in reducing the expression of resistance genes (MDR1and ABCG2 genes) in breast and lung cancer cells was investigated in three-dimensional (3D) cell culture.

Methods: XN from Humulus lupulus was purified using preparative-TLC method and confirmed by FT-IR and H-NMR methods. Spheroids of breast cancer (MCF-7) and lung cancer (A549) cell lines were prepared by drop hanging method. IC50 of XN was determined by MTT assay. Then expression of MDR1and ABCG2 genes were evaluated by qRT-PCR technique in 3D cell culture conditions under treatment with XN. The effect of XN on the cell cycle and apoptosis of cells treated by annexin kit were checked.

Results: The IC50 of XN was determined under 3D condition of MCF-7 and A549 cell lines, 12.37 µM and 31.17 µM, respectively. Treatment of cells with IC50 in 3D culture could significantly increase the sub-G1 phase in the cell cycle and apoptosis in both cell lines. Also, XN was able to significantly decrease the expression of ABCG2 and MDR1 genes in A549 cell line $P < .01$ and also significantly decrease ($P < .01$) MDR1 gene expression and ABCG2 gene expression in MCF-7 cell line ($P < 0.05$).

Conclusion: According to the obtained preliminary results in this study and by performing additional tests in the future, XN can be introduced as a natural compound in reducing the resistance of cancer cells.

Keywords: Xanthohumol, 3D cell culture, Resistance genes, Anticancer agents

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Transferring mitochondria as a surviving agent from Mesenchymal stem cells (MSCs) to differentiated cells by tunneling nanotubes (TNTs) (Review)

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Introduction: Mesenchymal stem cells are multipotent cells that possess properties such as self-renewal, differentiation potential, and migration to other sites of the body. This migration is intended for various purposes. One of these is the migration to heal the damaged cells by injecting them with a survival factor. This injection is facilitated through tunneling nanotubes (TNTs) that have some types like closed-end and opened-end ones. Tunneling nanotubes are F-actin-based connections between animal cells and transporting various cellular cargoes. They were discovered approximately 18 years ago and are capable of transporting nuclear components, macromolecules, and organelles like mitochondria. Mitochondria, known as the cell powerhouse, serve as the survival agent for damaged cells. It also has many roles in a big area of LIFE including essential metabolisms for construction and death order for destruction. Stem cells transfer mitochondria to these cells using tunneling nanotubes, allowing them to reestablish vital metabolic processes such as oxidation phosphorylation (OXPHOS) and the death cascade.

Methods: Research purposes: Many studies have been conducted on stem cells and their abilities for regenerative medicine and cancer therapy, the mechanisms, and their capabilities. There are some varieties of stem cells that originate from different organs and various stages of evolution such as the embryo stage and the adult stage. Given the current focus on this field of medical science, we are intrigued by the healing secrets that lie within cycle mechanisms, chemical pathways, and specific organelles like mitochondria. This study shows the relationship between sending mitochondria to the damaged or repair-need-target cells from mesenchymal stem cells (MSCs) by TNTs and surviving action of these mitochondria in the target cells. We emphasize on the surviving act of these bacteria-derived within the new host cell.

Results: After MSCs migrate and settle in the target site, chemical signals are required to be received from damaged cells and sent by stem cells. Cell-to-cell communication is vital for bigger effects like repairing and regenerating the injured tissue. There are some routes between cells to communicate with each other such as gap junctions, exosomes, secreted microRNAs, and tunneling nanotubes (TNTs). De novo F-actin-based tunnels grow up towards the cell intention for connecting to the target cell. These tunnels are going to be the highways for transporting healing factors to the damaged cells. The mitochondria of the MSCs in the target cells play essential roles in reviving and reprogramming the vital cycles of important molecules like ATP and calcium ions.

Conclusion: Animal models and human clinical trials show the successful implementation of MSCs from both human and non-human derived ones to repair damaged tissue clearly. The MSCs are collected from many sources such as bone marrow (BM), placenta, amnion, umbilical cord (UC), cord blood (CB), and peripheral blood (PB). These MSCs are migrating to the damaged tissue and have many effects on the targeted cells like releasing cytokines and immunomodulatory agents, transferring organelles to restore natural cell functions, and differentiation into target-like cells. These steps contribute to tissue regeneration, a topic extensively discussed in regenerative medicine. It is hoped that these studies will lead to the development of genetically modified mesenchymal stem cells that can specifically repair and revive thousands of different types of cells at the cellular and molecular levels.

Keywords: Mesenchymal stem cell (MSC), Tunneling nanotube (TNT), Mitochondria, Regenerative medicine

Treating Chronic Myeloid Leukemia with hit CRISPR Therapy (Review)

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Introduction: Introduction and aim: With the development of medications that target oncogene-encoded proteins over the past 20 years, the treatment landscape for a number of cancers has undergone a significant transformation. When the proteins that are encoded by oncogenes are suppressed by particular medications, the tumoral process can be halted or reversed. Oncogenes play a crucial role in human cancer. This can be shown in the case of chronic myeloid leukemia, when one oncogene is responsible for all of the clinical characteristics. Thanks to an inhibitor that was rationally created, the majority of individuals with this condition today enjoy a normal life expectancy. The oncogene is unchanged, the medicine just stops the protein, and only a small percentage of patients can choose to stop their treatment. With the development of genome-editing nucleases, particularly the CRISPR/Cas9 system, it is now possible to eradicate oncogenes. A brand-new therapeutic instrument has been created with virtually no limitations for the treatment of cancer. Recent research supports the idea that the CRISPR/Cas9 system might be the only effective treatment for chronic myeloid leukemia. This study examines the biology of chronic myeloid leukemia as well as the development of the CRISPR system and its potential as a targeted treatment for this condition. This study's objective was to treat chronic myeloid leukemia using CRISPR technology.

Methods: Search Method: The current study with titled Treating Chronic Myeloid Leukemia with CRISPR Therapy by searching scholarly databases such as Google Scholar, Science Direct, Springer, and PubMed for investigating CRISPR in leukemia.

Results: Results: Most of the characteristics of chronic myeloid leukemia are controlled by the constitutively active tyrosine-kinase BCR/ABL1 oncogene, which also plays a critical role in the development and maintenance of the disease. Tyrosine-kinase inhibitors are the first-line treatment for this reason, giving the majority of patients a life expectancy comparable to that of a comparable healthy person. Even though this causes side effects in many people, lifetime oral treatment is necessary because the oncogene is still there. Leukemic stem cells also continue to do nothing, and about 25% of patients exhibit resistance. New therapeutic options are still required as a

result. In this case, stopping or removing the oncogenic sequence might be a good treatment choice. Because it can cause a specific DNA double strand break, the development of CRISPR (clustered regularly interspaced short palindromic repeats) technology can provide a conclusive cure. Additionally, it offers complete and long-lasting oncogene deletion, whereas tyrosine kinase inhibitors (TKIs) only guarantee inactivation of the BCR-ABL1 oncoprotein during treatment. Prior to the development of CRISPR/Cas9, it was impossible to turn oncogenes off in humans because CRISPR/Cas9 breaks DNA in a sequence-specific way.

Conclusion: Conclusions: The ability of the CRISPR/Cas9 system to repair acquired mutations in a human myeloid leukemia cell line was originally shown in 2015 by Valletta et al. After that, CRISPR-Cas9 was effectively applied to animal models of genetic disorders. Finally, in 2016, the first CRISPR-Cas9 clinical trials in humans got underway. Chia-Hwa Lee et al. demonstrated a decreased proliferation rate as a result of BCR/ABL1 disruption in 2020 by disrupting ABL1 in the human CML K562 cell line utilizing a CRISPR/Cas9 lentiviral vector. As a result, according to the development of the CRISPR technique and the studies carried out, it can be said Creating an animal model with many genetic modifications used to be a time-consuming and expensive operation, but techniques like CRISPR-Cas9 now make it possible to introduce multiple mutations at once.

Keywords: CML; genome editing, cancer

Treating the effects of solanine poison in potato by the flavonoid in Mahoor flower (Review)

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Introduction: All organs of the potato plant contain two glyco alkaloids, alpha-solanine and alpha-chaconine, which are known as solanine poison. The permissible amount of solanine is 200 mg per wet weight of potato. This poison, which has pesticidal properties, causes the death of plant pests and acts as a natural defense mechanism for plants and is associated with plant resistance against Colorado potato beetle and potato leaf eater. Consuming a small amount of solanine and its derivatives initially causes pain and nervous problems such as diarrhea and vomiting, confusion, headache and itching. Consuming it in large quantities is dangerous for animals and humans and causes inflammation of the stomach and intestines and even death. Also, other risks of solanine are infertility, skin inflammation, hallucinations, fever and paralysis. These symptoms usually appear 8 to 12 hours after consumption, but in some cases, symptoms may appear quickly and after a few minutes after consuming high amounts of solanine. . Light, heat, germination and mechanical impact can increase this toxin, but humidity decreases its amount. The taste of this poison is characterized by burning mouth and throat.It has been said that the amount of solanine poison does not change much as a result of cooking and it is amount remains constant even up to 95%. this poison remains unchanged by frying in oil at 180 degrees Celsius,and if the same oil is used several times,the poison mey enter other foods. Therefore,the used oil should not be reused.In order to keep the level of glycoalkaloids in the potatoes low,keeping them in the light,in plastic bags and at a temperature of 7 degrees Celsius seems to be effective. Research has shown that the flavonoid in the mahor flower can be used yo treat complications caused by solanine poisoning. "Verbascum t hupsus" known as "Mullin" is a plant belonging to the monkey flower family and one of the med,icinal plants that is known in different regions as rabbit grass,rabbit flower, Mahor flowerand Mahor grass. This plant has been used since ancient times in traditional medicine to treat colds,angina and bronchitis,nervous disorders, anxiety,heart rhythm disorders and stomach discomfort as well as joint pain. This plant is also used to treat skin injuries. The anti-inflammatory

effect of this plant is due to the presence of compounds such as flavonoids, saponins and ribascoside compounds. Flavonoids are various compounds that occur naturally in many fruits and vegetables. They are also in herbal products such as tea. . Flavonoids are rich in antioxidant activity and can help the body eliminate daily toxins, and in addition to antioxidant and anti-inflammatory activity, they are related to skin protection, brain function, blood sugar regulation, and blood pressure. . Due to its anti-inflammatory and antioxidant properties, this flower can be used to treat the effects of solanine poison.

Methods: In this research, plant extraction is done by a rotary evaporator . Then, in order to identify the compounds and also to separate them, a high performance liquid chromatography device "HPLC" will be used. Then by adding Oserin cream, our therapeutic ointment will be made. The ointment made is tested on mice poisoned with solanine poison found in potatoes, and it is hoped that this research will be successful.

Results: Considering the antioxidant properties of the flavonoid found in Mahor flower, we can hope that the ointment obtained from the extract of this plant will be useful in treating the effects of solanine poison.

Conclusion: This project is still an idea and has not reached the implementation stage, but we hope that the ointment made with the extract of the Mahor plant with antioxidant and anti-inflammatory properties will be effective in improving the complications caused by the solanine poison found in potatoes.

Keywords: Mahor flower- solanine toxin-flavonoid-potato-glyco alkaloids

Treatment of Acute Myeloid Leukemia in Children by CAR-T Cell Therapy: A Promising Approach (Review)

Zahra Fathi,[1] Ehsan Rezaie,[2,*]

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2. 2 Molecular Biology Research Center, Systems Biology and Poisoning Institute, Baqiyatallah University of Medical Sciences, Tehran 1435916471, Iran

Introduction: Title: Treatment of Acute Myeloid Leukemia in Children by CAR-T Cell Therapy: A Promising Approach Zahra Fathi , Ehsan Rezaei * 1 Biotechnology, Department of Biology, Faculty of Basic Science, University of Ale Taha, Tehran, Iran 2 Molecular Biology Research Center, Systems Biology and Poisoning Institute, Baqiyatallah University of Medical Sciences, Tehran 1435916471, Iran Abstract: Acute Myeloid Leukemia (AML) is a complex hematological malignancy primarily affecting children. The current standard of care for AML includes chemotherapy, stem cell transplantation, and targeted therapy. However, the clinical outcomes often remain suboptimal, highlighting the urgent need for novel therapeutic approaches. Chimeric Antigen Receptor T-cell (CAR-T) therapy has emerged as a transformative treatment modality in various malignancies. The success of CAR-T therapy in pediatric leukemia, particularly in B-cell precursor Acute Lymphoblastic Leukemia (ALL), has encouraged exploration of its potential in AML. This article aims to review the current state-of-the-art clinical research and advancements in utilizing CAR-T cell therapy for treating pediatric AML. By targeting specific cell surface antigens expressed on leukemic blasts, CAR-T cells harness the immune system to recognize and eliminate cancer cells. High response rates, sustained remissions, and improved overall survival rates have been observed in preclinical and early-phase clinical trials utilizing CAR-T cell therapy in pediatric AML patients. However, several challenges, including antigen selection, antigen escape, cytokine release syndrome, and neurotoxicity, must be overcome to ensure the long-term efficacy and safety of CAR-T cell therapy for pediatric AML. In addition, the cost-effectiveness and scalability issues associated with delivering personalized CAR-T therapies demand further investigation. Overall, CAR-T cell therapy represents a promising therapeutic strategy for pediatric AML, holding immense potential in revolutionizing the treatment landscape of this aggressive disease. Future research should focus on refining CAR-T cell manufacturing techniques, optimizing antigen selection, and implementing

combination therapies to further enhance the clinical outcomes of this innovative treatment modality.

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By targeting specific cell surface antigens expressed on leukemic blasts, CAR-T cells harness the immune system to recognize and eliminate cancer cells. High response rates, sustained remissions, and improved overall survival rates have been observed in preclinical and early-phase clinical trials utilizing CAR-T cell therapy in pediatric AML patients. However, several challenges, including antigen selection, antigen escape, cytokine release syndrome, and neurotoxicity, must be overcome to ensure the long-term efficacy and safety of CAR-T cell therapy for pediatric AML. In addition, the cost-effectiveness and scalability issues associated with delivering personalized CAR-T therapies demand further investigation. Overall, CAR-T cell therapy represents a promising therapeutic strategy for pediatric AML, holding immense potential in revolutionizing the treatment landscape of this aggressive disease. Future research should focus on refining CAR-T cell manufacturing techniques, optimizing antigen selection, and implementing combination therapies to further enhance the clinical outcomes of this innovative treatment modality.

Keywords: Cancer, Leukemia, Immunotherapy, children

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Treatment of ATTR by CRISPR/CAS9 Through the Gene Editing (Review)

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3. Gorgan University of Agricultural Sciences and Natural Resources

Introduction: transthyretin amyloidosis (ATTR) is a fatal disease which is caused by the deposition of amyloid fibrils that is included of misfolded protein in different tissues and organs. additionally, TTR, a major amyloid-genic protein, is primarily produced in the live but also in other tissues which are included choroid plexuses of the brain(1), retinal pigment epithelial (RPE) cells of the eye, and α-cells of pancreatic islets. furthermore, TTR is predominantly synthesized by hepatocytes and circulates as a homotetrameric complicated that functions as a transporter for thyroxine and vitamin A . There are 2 distinct types of ATTR: hereditary or mutated (mt-ATTR) and wild-type (wt-ATTR0). Deposition of wild-type (wt) ATTR generally happens in older patients, giving rise to wt-ATTR amyloidosis, formerly known as senile systemic amyloidosis(2). Mt-ATTR is a rare autosomal dominant condition caused by mutations in the TTR gene with considerable heterogeneity in disease presentation; Amyloid formation in ATTR is thought to happen when disconnected transthyretin (TTR) monomers misfold and collect into amyloid fibrils, with amyloid-genic mutation in the TTR gene providing the dissociation of the tetramer into monomers. Roughly, about 100 disease-causing TTR gene mutations have been reported; some scientists support the idea that to be related with particular phenotypes, however, considerable variability exists among patients. Recently, the clustered regularly interspaced short palindromic repeats (CRISPR)-related protein 9 (Cas9) system is renowned as one of the most revolutionary biological instrument. This method includes two components: the first section is that a nuclease protein Cas9 that binds to DNA and initiates double-strand breaks (DSBs), and the second one is a very shot single guide RNA (sgRNA) that directs the Cas9 nuclease to the aimed genomic locus(3). according to The research treatment agent used, for treating ATTR, it consists of NTLA-2001, is basically related to the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and associated Cas9 endonuclease (CRISPR-Cas9) system, ‘molecular scissors’ that can delete a specific disease-causing mutation at an exact location in the DNA, therefore gene function will be modified. what is more, in recent years, it has been discovered that CRISPR-Cas9 has been used to alter cells outside the body in patients with sickle cell anemia and beta-thalassemia(4).

Methods: In 1987, Ishino et al. 30 noticed in Escherichia coli, the presence of a cluster of repetitive DNA sequences separated by variable spacer regions. Later, Mojica et al identified identical type of repeated sequences in numerous bacteria and archaea and named them Clustered Regularly Interspaced Palindromic Repeats or CRISPR. 31 Interestingly, the biggest breakthrough came in 2005 when the same group realized that these spacer sequences were from unknown ori- gin. 32-34 Together with the observation that many CRISPR-associated (Cas) genes encode proteins with putative nuclease and helicase do- mains, it was postulated that CRISPR may constitute an adaptive immunity system 33-36 by using RNAs as memory signatures of previ- ous infections.CRISPR mechanisms are very diverse but can be mainly classified into two distinct classes, class 1 and class 2, depending on the orga- nization of the effector protein complex. Class 1 comprehend three different types I, III and IV that are further subdivided into 15 sub- types. Distinct from class 1, that is characterized by the presence of a multi-protein effector complex, class 2 is defined by a single-pro- tein effector module. This class is divided into types II, V and VI. 43 The other CRISPR systems have been extensively reviewed else- where. 44,45 In CRISPR type II, DNA from viruses or plasmids of pre- vious infections is cut into small pieces and integrated into a CRISPR locus amongst short repetitive sequences (30-40 bp) separated by equally short spacer sequence.There are different approaches to generate isogenic disease mod- els in iPSCs using the CRISPR/Cas9 system.

Results: This first-ever human trial with the investigational CRISPR/Cas9-based in vivo gene editing therapy NTLA-2001 showed a significant and consistent reduction in serum TTR protein levels after a single admission and was generally well tolerated, representing a potential new option for the treatment and improvement of prognosis of cardiac ATTR amyloidosis. Continued monitoring of whether knockout of the TTR gene results in sustained TTR reduction over the long term is required. Evaluation of the potential effects of markedly reduced TTR levels on patients' clinical outcomes, with a focus on functional capacity, quality of life, andmortality benefits are essential.

Conclusion: The CRISPR/Cas9 RNA-guided DNA endonuclease system is a ver- satile technology that has rapidly transformed genome editing andbasic science research. The development of improved CRISPR/ Cas9 tools with high degree of DNA specificity, increased selectiv- ity and low level of by-products made this technology accessible to researchers worldwide to study human diseases. For example, it is now feasible to generate in vivo animal models of specific diseases in a few weeks. It is now possible to envision the treatment of genetic diseases in the near future using this technology. In fact,

several clin- ical trials using CRISPR/Cas9 approach to treat human genetic dis- eases are underway.

Keywords: CRISPR/ Cas9, ATTR/ Transthyretin amyloidosis, mutations, gene editing, treatment

Treatment of cervical cancer caused by HPV review article (Review)

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2. M.sc student of Microbiology Islamic Azad University Central Tehran Branch,Iran,Tehran

Introduction: HPV is a double-stranded DNA tumor virus known to cause cancers of the anus, oropharynx, penis, and cervix. How can cervical cancer be prevented?The most effective ways to prevent cervical cancer are to vaccinate girls against HPV, before their first sexual contact, and to screen women aged 30- 49 years or according to the national guideline. vaccines have shown promising results in recent years , the implementation of universal HPV vaccination strategies is expensive for developing countries, especially for populous countries such as China and India, and the multivalent vaccines cannot completely cover all the major types of HPV infections in these countries. Due to the huge economic burden posed by cervical screening and vaccination programs, many women in both developed and developing countries are still unprotected from HPV infections and its related cervical cancers. Key Factors that Contribute to HPV Persistence and Cervical Carcinogenesis: Host Susceptibilities to Latent HPV Infections and Cervical Cancer Like many other types of malignancies, cervical cancer is a chronic complex disease caused by a combination of inherited genetic factors and external environmental influences.

Methods: Key Factors that Contribute to HPV Persistence and Cervical Carcinogenesis: Host Susceptibilities to Latent HPV Infections and Cervical Cancer Like many other types of malignancies, cervical cancer is a chronic complex disease caused by a combination of inherited genetic factors and external environmental influences. Obvious evidence of genetic factors contributing to cervical carcinogenesis can be proved by warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis syndrome (WHIM) and hereditary nonpolyposis colorectal cancer (Lynch) syndrome, two autosomal dominant genetic disorder characterized by extensive HPV infection and high risk of cervical cancer. Although HPV infection may be the triggering factor, studies showthat a linkage between genetic factors and immune functions are correlated to cervical carcinogenesis and infection by themajor subtypes of high-risk.A small fraction of people infected with the type of high-risk HPV will develop cancer, which usually arise many years after initial infection. There are several approaches to screening for cervical cancer,

including cytological testing (Pap test), HPV DNA testing for high-risk strains of the HPV virus, and visual inspection of the cervix with acetic acid (VIA), with or without magnification.

Results: There are several approaches to screening for cervical cancer, including cytological testing (Pap test), HPV DNA testing for high-risk strains of the HPV virus, and visual inspection of the cervix with acetic acid (VIA), with or without magnification. Cytological testing is the most common screening method in developed countries, but it requires trained technicians and good laboratories that are often unavailable in developing countries. Effectiveness of Screening Methods All HPV screening methods, when done properly, can detect most precancerous lesions; none, however, is perfect.Even in developed countries, the results of Pap tests are much less reliable than many people realize.

Conclusion: The oncogenes of high-risk HPVs are retained and expressed in HPV induced cancers and their expression may have effects on the tumor microenvironment (TME).In contrast to the immune suppressive activities seen in HPV infection, HPV induced cancers such as head and neck squamous cell carcinomas (HNSCC) often demonstrate increased infiltration and activation of multiple immune cell types within the TME, indicative of an immune-hot phenotype.

Keywords: HPV, Cervical cancer , HPV vaccine

Treatment of genetic diseases using stem cells (Review)

Meshkat Torkashvand,[1,*]

1. nothing

Introduction: Genetic diseases are diseases that a person is born with and its symptoms appear at any age depending on the type of disease, and one of the most efficient and safe ways to treat it is using stem cells. Genetic diseases such as; Hereditary diseases focused on dry skin, childhood neurological disorders, Duchenne muscular dystrophy and myotonic muscular dystrophy, coronary artery disease, dilated cardiomyopathy, congenital defects in the production or function of blood cells, metabolic diseases, beta thalassemia ,Genetic immunodeficiency, cancer, hemoglobinopathy, genetic bone problems, cartilage repair, autoimmune disorders, and heart and nerve diseases can be treated using stem cells. Stem cells exist in most parts of the body and have the ability to self-replicate and differentiate into multiple lineages, and treatment by these methods is the result of the advancement of regenerative medicine.

Methods: This is a research and review with PubMed, Google, Springer, Science Direct, Disease Information Search and Sciencehub that focuses on the treatment of genetic diseases using stem cells.

Results: Somatic stem cells help in tissue regeneration, including in burns and severe injuries in patients suffering from life -threatening immunodeficiencies, in which stem cells are isolated and genetically manipulated outside the body and re-infused. For example, the efficacy of SCAD gene therapy in severe combined immunodeficiency of adult epidermal stem cells in vivo. They have the capacity to renew the epidermis, covering, differentiating and protecting our body, which can be a replacement for damaged skin. Human nerve cells cannot be studied due to their unavailability, but with cell programming techniques, a new source of human cells can be prepared for laboratory research. Induced pluripotent stem cells are a method that can differentiate into specific neuronal subgroups such as: dopaminergic, motor, inhibitory GABAergic and cortical neurons. Duchenne muscular dystrophy is a neurological disorder that causes progressive muscle weakness and atrophy, and the most common and severe type is DMD, in which 1 in 3,500 to 5,000 boys have a mutation in the X chromosome gene responsible for dystrophin. , which is a coding generator. It provides both management support and investment. The use of therapeutic cells is based on stem cells that use myoblasts, satellite cells, marrow and bone cells,

mesoangioblasts and finally HPSC cells from CD 133. The main nature of mesenchyme and non-mesenchyme is different and they differ in terms of lineage, culture conditions, important factors and surface markers. Correction of a genetic disease by gene editing mediated by CRA SPR-CAS9 in spermatogonial stem cells of SCT stem cell transplantation and for the treatment or improvement of a wide range of genetic diseases from inherent defects in blood cell production or function to metabolic diseases that They are mainly used to affect solid organs. Spermatogonial stem cells can produce multiple male gametes after transplantation into the recipient's testes, and it is a valuable approach for gene therapy and continuous production of genetically modified cells.

Conclusion: All methods found to treat diseases and genetic defects using stem cells are under research, but many of them have already been successfully registered. During the last few years, the rapid development of isolation and differentiation techniques has been noted in order to achieve effective transplantation results of myogenic HPSC cells. Mesenchymal and non-mesenchymal stem cells have immunoregulatory capacity, elicit immunosuppressive effects, and are immune privileged due to low expression of MHCII stimulatory molecules on the cell surface. To use stem cells in regeneration and repair, one must know information about their origin, fate and functional ability. So far, 7718 clinical trials based on stem cells have been registered in the databases of the National Institutes of Health of the United States of America until January 25, 2020, of which 3015 trials have been conducted and had favorable results, and it should be noted that these trials are similar to studies based on HSC and MSC is in progress.

Keywords: Stem Cells. Muscular dystrophy. mesenchymal stem cell. Spermatogonial. Somatic cells.

Treatment of Neurological Diseases by Stem Cells: ALS and Parkinson (Review)

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Introduction: Neurodegenerative diseases are caused by the loss of nerve cells. such as Parkinson's disease, Alzheimer's disease, Huntington's disease, Multiple sclerosis (MS) and Amyotrophic lateral sclerosis (ALS). These diseases can be congenital or acquired. Early diagnosis and treatment is the most effective way to treat this disease. Stem cells have been suggested as candidate therapeutic tools for neurodegenerative disorders, given their ability to give rise to the appropriate cell types after grafting in vivo. Parkinson’s disease (PD) is a very common neurodegenerative disorder that affects more than 2% of the population over 65 years of age. PD is characterized at a pathological level by a progressive degeneration and loss of: (1) nigrostriatal and mesolimbic dopaminergic neurons, leading to tremor, rigidity, and hypokinesia, the classical symptoms of the disease (2) noradrenergic neurons of the locus coeruleus , involved in the progression of the disease, dementia, and depression and (3) serotonergic neurons of the raphe obscurus and medial raphe, also involved in the symptoms of depression, often associated with PD.Several medications can help manage the symptoms of Parkinson's disease. These include levodopa, dopamine agonists, MAO-B inhibitors, and COMT inhibitors. Amyotrophic lateral sclerosis is a neurodegenerative disorder of upper and lower motor neurons, characterized by progressive muscular atrophy and weakness which culminates in death within 2–5 years. The etiology of neuronal atrophy is unknown, and there is no causal or treatment to slow disease progression. Two drugs, riluzole and edaravone, reduce the course of the disease. Riluzole reduces glutamate toxicity and increases life expectancy by about three months. The drug edaravone has recently been approved, but no report has been given about its positive effect on the patient's life span.

Methods: PD has long been considered to be one of the most promising target diseases for cell-based therapy. Indeed, numerous clinical and preclinical studies using fetal cell transplantation have provided proof of concept that cell replacement therapy may be a viable therapeutic approach for PD. Clinical studies have shown that transplanted fetal nerve tissue can lead to significant improvements in Parkinson's disease. recently postulated that stem cell therapy could potentially target several mechanisms responsible for the etiology of ALS and other nervous system disorders, and could be

regarded as one of the most promising therapeutic strategies for ALS treatment.There are two basic methods for stem cell transplantation: Systemic and local. One of the known systemic routes is intravenous delivery, which has a less invasive approach, but it is not known whether the injected stem cells can cross the blood-brain barrier or not.

Results: In Parkinson's disease lthough the source of embryonic tissue for transplantation has its own limitations and ethical issues, human parthenogenesis stem cells are a good alternative for this procedure because they are separated from the unfertilized egg and do not need to destroy the human embryo and can be used to generate an unlimited supply of nerve cells. In ALS , establishing standardized protocols for cell preparation and transplantation will help generate accurate and reproducible data for future preclinical and clinical studies.

Conclusion: To get an acceptable result and protect the nervous system, it is important to pay attention to several things: 1. Choosing the right cell type 2. Choosing the right cell source 3. Delivery route 4. Avoid suppressing the immune system. It should also be noted that the injected cells do not cause tumor formation in the body.

Keywords: Neurodegenerative diseases - Parkinson disease -ALS - Stem cells

ULK1 and its regulatory non-coding RNAs in drug resistance of multiple myeloma (Research Paper)

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Introduction: Multiple myeloma is defined as the second most frequent Hematological malignancy which is associated with a wide range of drug resistance. One of the mechanisms of resistance is the development of protective autophagy. This study aims to compare the relative levels of expression of ULK1, LC3B, SQSTM1, miR-26a-5p, miR-1297, lnc MALAT1 and lnc SNHG6 between U266B1cell line and bortezomib resistant myeloma cells.

Methods: The U266B1 cell line and plasma cells which were obtained from bone marrow of refractory patients were cultured in RPMI-1640 medium under optimal conditions. The relative expression of genes was determined using the real-time PCR. Data were statistically analyzed using the GraphPad Prism 8 software.

Results: In resistant cells, the expression of ULK1, LC3B, SQSTM1, miR-1297, lnc MALAT1 and lnc SNHG6 increased significantly, whereas miR-26a-5p didn't change significantly.

Conclusion: Since the autophagy process plays a key role in the development and maintenance of drug resistance in myeloma, analyzing the

expression of the genes involved in this system and their regulatory non-coding RNAs will aid in the discovery of potential cellular weaknesses and the management of drug resistance.

Keywords: multiple myeloma, drug resistance, ULK1, miR-26a-5p, miR-1297, lncMALAT1, lncSNHG6

Understanding the Gut Microbiome's Impact on Colorectal Cancer: From Development to Treatment Response (Review)

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Introduction: As one of the most common cancers in the world and the leading cause of cancer-related death in the world, colorectal cancer is the third most common cancer worldwide. Recent research has revealed that the gut microbiota has a significant impact on both the susceptibility to colorectal cancer (CRC) as well as the progression of the disease. Through the modulation of processes such as inflammation and DNA damage, as well as the production of metabolites that are capable of inhibiting or promoting tumor growth, this influence is attained. It has been reported that patients with CRC have dysbiosis of their gut microbiota, which is manifested by a reduction in beneficial butyrate-producing bacteria; the number of harmful opportunistic pathogens causing inflammation has increased. Metabolism is altered in CRC due to the altered production of bacterial metabolites, among them are polyamines and short-chain fatty acids. This review summarizes data on how gut microbiota influences colorectal cancer development. In addition, bacterial metabolites impact CRC development, and specific dietary factors affect the gut microbiota as well as the likelihood of developing colorectal cancer.

Methods: Four global databases (PubMed, Web of Science, Scopus, and Google Scholar) were searched. The search process was accomplished using keywords such as “colorectal cancer”, “gut microbiota”, “bacterial metabolites” and ” dietary mediators”, and 750 studies were funded. After removing duplicates and excluding ineligible reports, 100 articles were eligible to be included in this systematic review. Forty-four relevant articles with complete abstracts were included in the study.

Results: Research suggests that the gut microbiota might play a substantial role in colorectal cancer development by generating metabolites that interact with the immune system and release genotoxic(factor of virulence). Research

has shown that colorectal cancer patients have a reduced diversity of microorganisms and reduced bacterial richness in fecal samples and intestinal mucosa compared to their healthy counterparts. Moreover, colorectal cancer patients exhibit notable differences in distinct groups of bacteria, potentially influencing mucosal immunity. The prevalence of Streptococcus gallolyticus, Escherichia coli, Peptostreptococus, Shigella, Enterococcaceae or Campylobacter, Enterococus faecalis, Fusobacterium nucleatum, Enterococcaceae or Campylobacter, and Bacteroides fragilis in CRC patients is particularly high, while the prevalence of Clostridium, Roseburia, Faecalibacterium, Blautia, and Bifidobacterium decreases as well. The decline in bacteria that produce Butyrate can result in an increased number of pro-inflammatory opportunistic pathogens and imbalanced intestinal homeostasis (dysbiosis), leading to tumor formation. It has been shown that SCFAs (especially butyrate) Keep the intestinal barrier intact in colon cancer by regulating the immune response. The large intestinal fermentation of soluble fiber into SCFAs has been demonstrated to have anti-carcinogenic effects in colon cancer models in vivo. The consumption of high fiber can promote the growth of gut bacteria that produce butyrate. The addition of PUFAs, polyphenols, and probiotics to a primary prevention program may also be helpful in reducing the risk of CRC. Aside from enhancing treatment response and minimizing toxicity, intestinal microbiota can assist in cancer treatment. In the absence of dietary PUFA, polyphenols, and probiotics, fiber intake promotes butyrate-producing bacteria, which may reduce CRC risks. Adjuvants that improve and alleviate the toxicity of conventional CRC treatments can be derived from intestinal microbiota.

Conclusion: Colorectal carcinogenesis may be impacted by dysbiosis of the gut microbiota in several ways. By disrupting cell cycle regulation, synthesizing genotoxins, and generating harmful metabolites, pathogenic bacteria compromise the integrity of the intestinal epithelial barrier. It is also possible that some lysogenic bacteriophages found in the gut microbiota would indirectly contribute to tumor progression through bacterial lysis in the colon by affecting the bacterial population there. The gut mycobiota may also play a role in colorectal cancer development, as ecological analyses have revealed synergistic interactions among fungi, as well as antagonistic interactions between bacteria and fungi.

Keywords: colorectal cancer,gut microbiota,bacterial metabolites,dietary mediators

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Unleashing Bacteria-Based Therapy for Bladder Cancer: Recent Bioengineered agent and Bacterial-Derived Molecules (Review)

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Introduction: Bladder cancer poses a formidable global health challenge, necessitating a novel approach to therapeutic intervention. In response, bacteria-based therapies have emerged as promising contenders in this dynamic landscape. This review delves into the potential of bacteria-based therapy for bladder cancer, with a keen focus on the transformative roles of novel bioengineered agents and bacterial-derived molecules.

Methods: Articles related to bacterial therapy for bladder cancer, specifically in the context of bioengineered agents and bacterial-derived molecules, were screened on PubMed, Google Scholar, ScienceDirect, and other Current Contents databases. Priority was given to articles with free full-text access. Relevant and recent publications were meticulously analyzed, and pertinent materials were extracted for inclusion in this review.

Results: The spotlight of our findings rests on the potential of novel bioengineered agents, a class encompassing genetically modified bacteria and fusion proteins. This innovative approach holds promise for targeted tumor destruction, allowing precision in treatment. This form of therapy presents the prospect of personalized interventions, minimizing damage to healthy tissue while tailoring treatments for maximal therapeutic efficacy. The review underscores the potential of these bioengineered agents, notably genetically modified bacteria and fusion proteins, in achieving targeted and selective tumor-killing. Such agents offer the advantage of personalized treatment with minimal off-target effects, ensuring treatments are customized for optimal therapeutic outcomes. However, the utilization of these agents requires careful consideration of challenges, including optimizing dosages, managing potential long-term effects, and addressing the emergence of

resistance mechanisms. To enhance therapeutic effectiveness, the recombination of bacterial agents through genetic modifications emerges as a strategic avenue, promising synergistic benefits that augment tumor recognition, immune activation, and drug delivery capabilities. Additionally, bacterial-derived molecules, encompassing enzymes, antimicrobial peptides, toxins, and antibiotics, reveal diverse anticancer properties. These molecules hold potential in various aspects, from inducing apoptosis to inhibiting oncogenic pathways and activating antitumor immune responses. Such multifaceted properties highlight their potential as valuable therapeutic tools in the fight against bladder cancer.

Conclusion: Bacteria-based therapy represents a promising frontier in the battle against bladder cancer, offering multifaceted approaches through novel bioengineered agents and bacterial-derived molecules. Despite their potential, challenges including dosing refinement, long-term consequences, and resistance mechanisms require thorough investigation for safe and effective clinical translation. Recombination strategies hold promise in overcoming these challenges and enhancing therapeutic efficacy. The extensive potential of bacteria-based therapy calls for further research and rigorous clinical validation to fully unlock its benefits in bladder cancer treatment.

Keywords: Bladder cancer, bacteria-based therapy, novel bioengineered agents, bacterial-derived molecules

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Unleashing the Potential of In-Vitro Cell-Based Bioassays: From Fundamentals to Breakthroughs (Review)

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1.

Introduction: Biopharmaceuticals are a rapidly growing class of drugs that are derived from living organisms and are used to treat a wide range of diseases. In-vitro cell-based bioassays are an essential tool for evaluating the potency, efficacy, and safety of biopharmaceuticals during the drug discovery and development process

Methods: This article aims to offer an overview of the fundamentals, Development, and Application of In-vitro cell-based bioassay for biopharmaceuticals. A literature search was conducted on Scopus, PubMed, and Web of Science up to August 2022 for this purpose. We performed a title/abstract/keywords search for "Cell-based assay," "Bioactivity," ", In-vitro bioassay," "Potency Testing," and "Biopharmaceuticals".

Results: This manuscript provides a comprehensive review of the fundamental principles and methods of in-vitro cell-based bioassays for biopharmaceuticals, as well as the latest advances and applications in this field. We discuss the key factors that influence the design and performance of in-vitro bioassays, including the choice of cell type, the selection of relevant biological endpoints, and the optimization of assay conditions. We also highlight the challenges and opportunities in the development and validation of in-vitro bioassays for biopharmaceuticals, and provide examples of successful applications in drug discovery and development.

Conclusion: Overall, this manuscript aims to provide a valuable resource for researchers and practitioners in the field of biopharmaceuticals and drug development who are interested in using in-vitro cell-based bioassays to accelerate and improve the drug discovery and development process. Overall, this manuscript aims to provide a valuable resource for researchers and practitioners in the field of biopharmaceuticals and drug development who are interested in using in-vitro cell-based bioassays to accelerate and improve the drug discovery and development process.

Keywords: Cell-based assay, Bioactivity, In-vitro bioassay, Biopharmaceuticals, Peptides/Protein

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Unlocking NSCLC Therapeutics: EGFR, miRNA, and Molecular Docking in Drug Discovery (Research Paper)

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Introduction: Non-small cell lung cancer (NSCLC) represents a significant challenge in the field of oncology, necessitating novel therapeutic approaches for improved patient outcomes. This study explores the integration of microRNAs (miRNAs) and molecular docking techniques in the context of EGFR-targeted drug discovery for NSCLC. Epidermal Growth Factor Receptor (EGFR) has emerged as a pivotal player in NSCLC pathogenesis and a promising therapeutic target. MiRNAs, small non-coding RNA molecules, play a crucial role in regulating gene expression and are intricately connected to cancer-related signaling pathways. This research investigates the potential of miRNAs to modulate EGFR-related pathways, providing insights into their utility as therapeutic agents or targets. Molecular docking, a computational approach, is employed to analyze the interactions between miRNAs, EGFR, and potential drug candidates, offering a precise and efficient means of drug discovery. The results of this study shed light on innovative strategies for advancing NSCLC therapeutics, emphasizing the pivotal role of miRNAs and molecular docking in unlocking new avenues for drug development in the context of EGFR-targeted NSCLC treatment.

Methods: In our research, we undertook a molecular docking study involving the EGFR molecule and a set of 57 compounds. Initially, we accessed the three-dimensional (3D) structure of EGFR from the PDB database (PDB ID: 7jxq). Following this, we utilized Chimera 1.15 to remove any extraneous structural elements associated with our target molecule, thereby preparing it for the subsequent docking procedure. To create our unique ligands, we obtained compounds from the ZINC15 database, applying two specific filters: 'standard-ok' and 'world.' The 'standard-ok' filter encompassed substances with "standard" reactivity, including those adhering to PAINS and ZINC12 "clean" filters. Meanwhile, the 'world' filter comprised compounds that are approved drugs in major jurisdictions, including by the FDA (i.e., DrugBank approved). This comprehensive selection process yielded a total of 57 distinct

molecules. Subsequently, we converted these molecules into formats conducive to analytical procedures using the Open Babel software. Leveraging the PyRx program, we conducted our docking experiments through the Vina Wizard console. Following the docking phase, we diligently scrutinized our results, employing rigorous criteria such as Binding Affinity and root mean square deviation (rmsd), both in the upper-bound (rmsd/ub) and lower-bound (rmsd/lb) contexts, to meticulously refine our selection of compounds. We employed the miRDB website to identify ten miRNAs with the most elevated target scores for targeting EGFR.

Results: Considering the Binding Affinity and root mean square deviation (rmsd) metrics, we found that the three medications, namely, Imatinib, Ebastine, and Ibrutinib, demonstrated the most favorable outcomes. Remarkably, these results even surpassed the performance of the three officially approved drugs Vandetanib, Erlotinib, and Gefitinib in our evaluation.The miRNAs with the most elevated target scores are comprised of the following 10 : hsa-miR-141-5p, hsa-miR-6878-5p, hsa-miR-514a-3p, hsa-miR-4533, hsa-miR-514b-3p, hsa-miR-6867-5p, hsa-miR-7157-3p, hsa-miR-6737-3p, hsa-miR-7110-3p, hsa-miR-9985

Conclusion: In the pursuit of enhanced therapeutics for non-small cell lung cancer (NSCLC), this study has unveiled a multifaceted approach that integrates microRNAs (miRNAs), molecular docking, and the targeting of the EGFR. NSCLC, a formidable oncological challenge, demands innovative strategies to improve patient outcomes, and our research has contributed to this endeavor. The findings of this study emphasize the pivotal role of miRNAs in modulating EGFR-related pathways, providing valuable insights into their potential as therapeutic agents or targets in NSCLC treatment. The integration of molecular docking techniques has enabled a deeper understanding of the intricate interactions between miRNAs, EGFR, and potential drug candidates, facilitating the rational design and optimization of novel therapeutics.

Keywords: NSCLC, EGFR, miRNA, Molecular Docking, Drug Discovery

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Unlocking the potential of nutraceutical in celiac disease pathogenic cascade (Review)

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Introduction: Celiac Disease (CD) stands as the most typical hereditary food-induced intolerance worldwide. CD is a type of enteropathy that is chronic and caused by an autoimmune response. It typically affects individuals who are genetically susceptible, and it is often triggered by consuming gluten proteins from wheat, barley, and rye . Among autoimmune diseases, a highly prevalent one is celiac disease which affects 1% of people globally and is gradually increasing. Currently, the only known effective treatment for celiac disease is following a gluten-free diet (GFD). In the present study we reviewed the potential of different nutraceuticals in celiac disease pathogenic cascade.

Methods: A critical review article which hypnotize about potential of nutraceutical in celiac disease pathogenic cascade

Results: Phytochemicals, PUFAs, amino acids, vitamins, minerals were found to be potential for affecting celiac disease pathogenic cascade.

Conclusion: A regimen concluding different nutraceutical could be beneficial in celiac disease patients.

Keywords: Celiac- Nutraceuticals- Phytochemicals-Micronutrient

Using bioinformatics tools to identify genes involved in the virulence of Campylobacter jejuni chemostat-grown to S-nitrosoglutathione (Research Paper)

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Introduction: Campylobacter jejuni is the leading cause of bacterial foodborne gastroenteritis worldwide and represents a major public health concern. Moreover, an increasing body of evidence suggests a strong association between C. jejuni infection and Guillain-Barré syndrome, a peripheral nervous system disorder characterized by inflammatory demyelination. C. jejuni virulence factors include motility, chemotaxis, adhesion, and invasion.C. jejuni colonizes the small intestine and colon through the use of virulence factors such as motility, chemotaxis, adhesion, and invasion. A 2021 study identified 126 virulence factors in C. jejuni genomes from around the world. Overall, the virulence of C. jejuni is a complex process that involves multiple factors. Identifying the genes and factors involved in C. jejuni virulence is important for understanding the pathogenesis of this bacterium and developing strategies to prevent and treat infections.

Methods: The microarray data with the accession IDs GSE5396 were identified, extracted and analyzed by GEO2R online tools and R software. Genes with the highest differential expression were identified using parameters P<0.05 and LogFC>|1|. Subsequently, the expression of the related genes was isolated and for the genes that had an increase in expression, the protein network was predicted by STRING database and visualized with the Gephi software.

Results: By identifying different genes that had a significant decrease or increase in expression, it was found that a set of genes (hrcA, clpB, dnaK, grpE) are involved in virulence of C.jejuni. The (hrcA) gene was found to be an intrinsic protein thermosensor that represses its own promoter and the regulatory region controlling the transcription of other genes at temperatures up to 37°C. The (clpB) gene was found to play a vital role in the thermotolerance of Campylobacter spp. The (dnaK) and (grpE) genes were

found to be involved in the synthesis and modification of macromolecules. These findings suggest that these genes play important roles in the virulence of C. jejuni and could be potential targets for the development of interventions to prevent and treat infections.

Conclusion: Through comprehensive bioinformatics analysis of gene expression data, this study successfully identified differentially expressed genes in C. jejuni when exposed to chemostat-grown by S-nitrosoglutathione. These findings offer valuable insights into the intricate molecular pathways utilized by C. jejuni to sustain its survival, adapt to environmental stressors, and initiate infections. Moreover, this knowledge can contribute to the development of more potent control measures against infections and aid in the design of preventive strategies.

Keywords: Campylobacter jejuni, virulence, microarray, bioinformatics analysis, R software

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Using Microbiome for Cancer Diagnosis and Therapy (Review)

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Introduction: Numerous cancer types cause the death of 7.5 million individuals annually. Recent approaches have been developed to enhance tumor prognoses. Nonetheless, certain cancers continue to have unfavorable prognoses due to factors namely metastasis when diagnosed and limited treatment efficacy. These come with the persistent multiplicity of cancer-related fatalities. Bacteria maintain a persistent presence within the human body throughout its lifespan and beyond. The historical interconnection between the development of human diseases like cancer and the evolution of microorganisms, mainly bacteria, is widely interesting. A significant milestone involves recognizing that an altered microbiome is a notable hallmark of cancer. Consequently, the investigation of the microbiome alteration holds substantial promise as a subject of cancer research. The current study aims to review the microbiome as a therapeutic and diagnostic target in cancers.

Methods: An estimated population of 10^13 to 10^14 microbiota inhabit the gastrointestinal tract, despite other sterile tissues. The genetic material contained within the microbiome surpasses the extent of the human genome. It has been proposed that microbiome communities can impact on development, progression, formation of metastases, and responses to treatment of diverse cancer types. Furthermore, the interconnection between the microbiome and cancer metastasis can be a positive or negative relationship. Mounting evidence substantiates the premise that the gut microbiota can modify the immune system, given its role in harboring over half of the body's lymphocytes, potentially impacting the dissemination of cancer. On the other hand, the microbiome is thought to impede cancer metastasis through its anti-inflammatory attributes. Even, interventions targeting the structure of microbial metabolites can obstruct both the early and late stages

of cancer metastasis. Concisely, it has been substantiated that the initiation and progression of cancer can be influenced by dysbiosis of the microbiome.

Results: Critical roles in the metastasis of breast cancer, melanoma, prostate cancer (PC), and colorectal cancer (CRC) are played by microbiomes like Fusobacterium nucleatum(Fn), Porphyromonas gingivalis, and Akkermansia, as well as microbial metabolites including indole-propionic acid (IPA), cadaveric amines, and sodium butyrate (NaB). Metastasis promotion through inducing epithelial-mesenchymal transition (EMT) and activating the Wnt signaling pathway is facilitated by the microbiome, which, in turn, reduces β-linked proteins. Additionally, the microbiota upregulates E-cadherin expression through multiple mechanisms, impeding the EMT process. Moreover, intestinal microbiota-produced cadaveric amines suppress EMT, leading to the inhibition of cancer stem-cell motility and metastasis, thereby exerting a tumor-suppressive impact on breast cancer. A strong negative correlation was observed between the presence of Oscillatoria and the genes associated with promoting EMT, which is suggestive of potential metastasis inhibition in muscle-invasive bladder cancer (MIBC). The utilization of 16S RNA sequencing on lung tissue indicated a close relationship between the levels of Bacteriaceae, Trichospiraceae, and Ruminococcaceae within lung tissue and the risk of lung cancer, besides the survival outcomes of recurrence-free and disease-free survival among individuals diagnosed with lung cancer. A significantly higher abundance of F. nucleatum was observed in patients with CRC and its associated precancerous lesions compared to the control group. Moreover, F. nucleatum levels were notably elevated in both cancerous and para-cancerous tissues within the context of CRC. Alterations in the F. nucleatum to Faecalibacterium prausnitzii and Bifidobacterium ratio in stool samples from CRC patients hold potential as a means to detect early-stage CRC.

Conclusion: The microbiome holds a significant place within the human body through diverse functions. Research findings indicate its pivotal involvement in carcinogenesis, a role more substantial than initially anticipated. In conjunction with therapeutic approaches, clinical trials are currently being undergone by certain genetically modified bacteria, serving as antitumor agents, antioncogenes, or immunogenic antigens. It assists the enhanced potential of these bacteria for cancer therapy. With a comprehensive understanding of the microbiome, effective diagnostic and therapeutic approaches can be developed for the prevention, detection, and treatment of cancers. The microbiome is a remarkable entity from diagnosis to cancer therapy.

Keywords: Microbiome, Cancer, Diagnosis, Therapy

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Varicella zoster disease review article (Review)

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Introduction: Varicella zoster virus is a lipid-enveloped virus derived from the cell membrane. Varicella zoster virus is classified as a member of the herpes viride family and subfamily of the alpha herpes virus or herpes virine. Varicella zoster virus is the causative agent of two different diseases: chicken pox and shingles. Chicken pox is the primary infection that affects mostly children and is characterized by fever, blisters, and an itchy and painful rash, while herpes zoster is common in adults and in the third age. Varicella zoster virus is one of the human alpha herpes viruses that causes varicella and is generally called chicken pox. Herpes zoster (shingles) is an acute skin-nervous and febrile infectious disease caused by the reactivation of the varicella zoster virus. After primary infection (chicken pox) or vaccination, this virus remains latent in the cells of the sensory posterior root ganglion, and with the reduction of cellular immunity, the virus is reactivated and then replicates within the cells of the sensory posterior root ganglion. It migrates again to the sensory nerves of the skin and leads to herpes zoster, which is generally called shingles.

Methods: After primary infection (chicken pox) or vaccination, this virus remains latent in the cells of the sensory posterior root ganglion, and with the reduction of cellular immunity, the virus is reactivated and then replicates within the cells of the sensory posterior root ganglion. It migrates again to the sensory nerves of the skin and leads to herpes zoster, which is generally called shingles. Varicella zoster usually appears as a painful one-sided vesicular rash and causes this acute disease to last for 3 to 5 weeks and is usually seen in older people and immunocompromised patients. The incidence of varicella zoster varies based on population density, risk of exposure, social factors, humidity conditions and specific geographical regions of the world. Some of the complications caused by varicella zoster are: secondary skin infection, skin gangrene, septicemia, visceral distress, neuralgia after zoster, and numerous eye complications. The most common complication of zoster is chronic pain caused by neuralgia after herpes, which is seen in approximately 20% of people over 50 years old. Zoster is rarely fatal, but it causes long-term mental-psychological disorders, physical disabilities and sleep disorders.

Results: Medicines such as acyclovir, valciclovir, famciclovir, foscarnet and alpha interferon are usually used to treat varicella zoster. The main drug used to treat varicella zoster is acyclovir. Acyclovir is not allowed to be prescribed in the first trimester of pregnancy. Drugs such as Foscarnet and interferon alpha are approved drugs for the treatment of varicella zoster, and these drugs have shown a certain effectiveness in high-risk patients.

Conclusion: Genetic variation in human leukocyte antigens may increase the risk of zoster, and immune disorder and imbalance between anti-inflammatory and inflammatory cytokines may play a role in the reactivation of varicella zoster virus.

Keywords: Varicella zoster virus Shingles Chicken pox Herpes zoster Alpha herpes virus

Vibrio cholera and stool examination test review article (Review)

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Introduction: Cholera is an infection of the small intestine caused by some strains of Vibrio cholera bacteria.Its indicator is a lot of watery diarrhea.Acute and profuse diarrhea is a striking example of enteropathogenic invasion and disruption of the intestinal microbial community.The discoverer of cholera is Robert Kocht,a German scientist. The main reservoir is human cholera. People who have a weak immune system or people who take antacid drugs and whose stomach is less acidic are more vulnerable to this disease. . People who travel to endemic areas can be exposed to cholera and bring the Vibrio cholera bacteria into their region that is free of the disease. Vibrio cholera bacteria is also related to the type of blood group of people, and people who are blood group O. They are the most vulnerable.

Methods: Cholera outbreaks are more widespread in areas where there is poor sanitation and overcrowding, or where there is war or flooding. The toxin of Vibrio cholera bacterium is cholera toxin, which is an enterotoxin and belongs to the family of AB toxins. It has two subunits A, heterodimeric and subunit B, hemopentameric. Cholera toxin, by converting ATP to cAMP, causes the excretion of chlorine ions and inhibits the absorption of sodium ions. Vibrio cholera bacterium enters the intestinal mucosa and multiplies there. Then, by tearing itself, it releases poison and causes an increase in CAMP, which increases the leakage of water and electrolytes into the intestine, and prevents the absorption of electrolytes. During infection, Vibrio cholerae can form biofilms that play a role in disease transmission and pathogenesis. Vibriocholera is a facultative human pathogen and can be isolated from aquatic environments.

Results: Cholera diagnosis method is through stool test. The probability of death in the absence of treatment is 50 to 60%, and less than 1% in the case of full medical intervention.

Conclusion: The symptoms of the disease include excessive thirst, vomiting without nausea, watery and pressure-filled diarrhea without heartache that the patient cannot control, cramping of the muscles behind the leg, decreased urination, yellow urine. The duration of the disease varies from 2 to 5 days,

and each of the above symptoms alone does not indicate cholera, and the disease may not have all the symptoms.The main treatment for affected people is ORS. The first stage of treatment is drinking water and electrolytes. The next stage is the use of antibiotics. Antibiotics play a role in reducing the duration and severity of the disease and speeding up the cleaning of bacteria. But prescribing antibiotics is not necessary. The first choice is macrolide antibiotics. Resistance of Vibrio cholera to tetracycline and doxycycline has spread. Cefixime, ampicillin, azithromycin, and erythromycin are suitable for children and pregnant women.

Keywords: Vibrio cholera -immune system -watery diarrhea-cholera toxin-Robert Koch

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Vitamin D and Magnesium protects against Cadmium-induced fetus's pulmonary toxicity by reducing P53 and Foxo1 genes expression in Wistar rats (Research Paper)

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Introduction: Exposure of healthy mothers to contaminants containing heavy metals such as Cadmium (Cd) can lead to respiratory fetus defects followed pregnancy. This study investigated the therapeutic and protective role of Vitamin D and magnesium (Mg) in reducing the toxic effects of cadmium on the neonates born from exposed pregnant mothers.

Methods: 50 Wistar Rats were divided into Control, Cd, Cd +Vitamin D, Cd +Mg, and Cd +Vitamin D +Mg treatment groups. Cadmium injected to the Rats over a period of 28 days, subsequently mated, and pregnancy confirmed. The treatment carried out due to the 6th day of pregnancy to the 14th day. The activity level of liver enzymes in the collected serum samples was determined spectrometrically. ELISA was used to specify tumor necrosis factor-alpha (TNF-α) levels. Real-time PCR and western blotting were used to measure (P53 and Foxo1 genes) and (VEGF and BMP-4 proteins) expression. Hematoxylin and eosin staining were used to determine the histology of the lungs.

Results: The Cd+ Vitamin D+ Mg group had a statistically significant decrease in liver enzymes, TNF-α, P53, Foxo1, VEGF, and BMP-4 levels compared to the Cd. The bronchioles in Vitamin D+ Mg group were a normal appearance, and the rate of hemorrhage, inflammatory cell infiltrations, and the alveoli's wall thickness, were reduced compared to the Cd group.

Conclusion: It concludes that Vitamin D and Mg can be considered a protective combination in the Cd toxicology which able to repair and regenerate damaged lung tissue without any toxic effects on liver.

Keywords: Cadmium; Vitamin D; Magnesium; Lung Development

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Wether education has a positive impact on nurses' knowledge, attitudes, skills, and practices related to pain management . (Review)

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Introduction: Pain is a significant symptom associated with disease and injury, often driving individuals to seek healthcare assistance. Despite efforts made in the past decade to enhance pain management through research, technological advancements, and the availability of clinical guidelines, pain continues to be a persistent global health issue. Numerous studies have revealed that patients frequently do not receive appropriate pain management, leading to undertreated pain. One contributing factor to this problem is insufficient knowledge, particularly among nurses who play a crucial role in patient care. Unfortunately, studies conducted worldwide have identified deficiencies in nurses' knowledge and attitudes towards pain management. These knowledge and attitude gaps are often attributed to a lack of comprehensive pain education in nursing curricula resulting in graduates with inadequate knowledge. This review aims to provide an updated understanding of the impact of educating nurses on pain management .

Methods: The key words of nurse, education and pain management were searched in MEDLINE , AMED , EMBASE and PsychINFO databases and after applying the inclusion and exclusion criteria , 35 articles were selected and critically evaluated.

Results: The findings from the reviewed studies indicate that nurses have deficits in pain management knowledge and exhibit poor attitudes towards pain during the initial assessment . Some studies reported very low pre-test knowledge scores, while others had relatively high scores Another significant area where studies reported limited knowledge and low scores among nurses was in misconceptions regarding opioid addiction in pain management.Studies consistently demonstrate that nurses face ongoing challenges when it comes to addressing questions regarding the prevalence of addiction among opioid recipients . Three studies reported relatively low baseline scores, while two studies reported relatively high baseline scores. These differences in scores can be attributed to the participants' educational

background, as two of the studies with low scores noted that most participants had not received any pain education, either during their formal education or in clinical settings.While it is true that in many developing countries nurses do not have the authority to prescribe medication and rely on doctors' prescriptions, it remains crucial for nurses to possess knowledge about pharmacological pain agents, their proper administration, and management. This includes being well-informed about the potential side effects associated with these medications.When appropriate pain assessment tools are used, most children above the age of four can provide estimations of their pain intensity. However, due to the subjective nature of pain, the accuracy and acceptability of children's pain reports using pain scales can sometimes be questioned, especially if healthcare personnel's observations do not align with the child's self-reporting. Consequently, some nurses in this review expressed doubts about the reliability of children's self-reporting of pain. Another issue highlighted in the review findings is the long-term retention of knowledge following educational interventions. The goal of these interventions is to improve long-term pain management. It is crucial for participants to retain knowledge over extended periods so that it can be effectively applied in practice . Providing three to four-hour refresher courses on pain management to healthcare professionals at least once a year can help improve knowledge retention.One study mentioned in the review implemented a certification process for nurses who completed pain management training.

Conclusion: The objective of this review was to examine the impact of education on nurses' knowledge, attitudes, skills, and practices related to pain management . the findings of this review are significant as they shed light on issues related to long-term knowledge retention and persistent gaps in pharmacological pain management and opioid use. Some studies have indicated that these gaps persist even after educational interventions . Therefore, it is crucial to organize Continuous Professional Development activities focused on pain management for nurses at least once a year. It is important to note that the recommendation of once a year is not based on an evidence-based optimal time frame for ongoing pain education and should be further researched. Additionally, persistent misconceptions and knowledge gaps regarding pharmacological pain management were observed even after educational interventions. This suggests that some misconceptions are deeply ingrained and require repeated education to overcome. Therefore, when designing training programs for nurses, special attention should be given to these areas.

Keywords: nurse , education and pain management

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Zinc/Iron oxide nanocomposites: Green synthesis, characterization, and evaluation of their effects on anxiety in rats exposed to noise stress. (Research Paper)

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1. دانشگاه آزاد اسلامی واحد خمینی شهر

Introduction: Noise pollution is considered one of the products of the modern lifestyle that causes great damage to various systems of the body including the nervous system [1]. Noise pollution can cause stress leading to anxiety and depression. Noise stress also increases the immobility time, which indicates anxiety-like behavior [2]. To prevent the negative effects of noise stress on the auditory system, behavior, and mental health, ambient noise should not exceed 55 decibels during the day and 40 decibels during the night [3, 4]. Nowadays, interdisciplinary studies in nanotechnology have opened a new window of wonder in the world of science and knowledge, and have made the new principles of engineering and human understanding in the biological and medical sciences to undergo a novel transformation [5]. Extensive use of nanoparticles in various fields causes environmental pollution [6]. Due to their high permeability, nanoparticles easily cross the blood-brain barrier (BBB) and they can enter the human body in large quantities [7]. Therefore, these substances may cause negative effects on humans and other organisms than ordinary substances may do [8]. Destructive or beneficial effects of nanoparticles on cognitive function and psychological behavior have recently been the target of extensive studies [9]. Animal and human bodies respond to stress in two ways: a) rapid response, during which the autonomic nervous system (ANS) is activated leading to the secretion of the catecholamines epinephrine and norepinephrine in the adrenal gland, that results in typical symptoms of stress, and b) slow response, during which the hypothalamic-pituitary-adrenal (HPA) axis is activated, leading to increased secretion of corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) [10]. ACTH stimulates the adrenal cortex, giving rise to the secretion of glucocorticoids (GCs). The most important of GCs are cortisol in humans and corticosterone in rats (CORT) [11]. It is shown that exposing pregnant rats to noise stress for two to four hours/day increase serum corticosterone level [12]. Also, the serum level of corticosterone increases significantly in offspring exposed to maternal separation stress [13]. Oxidative stress, which is caused by an imbalance between the formation of free oxygen radicals and the inactivation of these species by the antioxidant defense system, can cause oxidative damage to various intracellular and extracellular molecules [14]. These detrimental

effects generally appear after exposure to a relatively large amount of reactive oxygen species (ROS). Oxygen radicals are generated in the body as byproducts of oxidative metabolism [10]. To protect the oxidative cycle and stability, cells have developed defense mechanisms that strike the right balance between antioxidant and oxidant molecules [15]. Zinc ions participate in the mechanisms of the enzyme superoxide dismutase, thus playing an important role in oxidative balance and anxiety control [16]. The effects of zinc and magnesium supplements on postpartum depression were investigated in a clinical study [17]. The results showed that magnesium and zinc reduced postpartum anxiety and depression [17]. As a reducing anxiety-like behavior factor, zinc oxide nanoparticles are more effective in reducing anxiety behaviors than conventional zinc oxide. It is also shown that iron oxide nanoparticles exerts a pronounced anti-anxiety effect in small amounts (1 mg/kg), however, its anti-anxiety effect decreases in large quantities (5 mg/kg) [16). Metal nanomaterials have various applications in the biological and medical sciences[18]. The effects of metal nanoparticles on variables such as stress and anxiety were investigated in this study. Due to their magnetic properties, high biocompatibility, and high catalytic ability, zinc/iron oxide nanocomposites are widely used in industrial, agricultural, and medical fields such as medical imaging, biotherapy, and photocatalysis [19]. Zinc and iron food supplements are also effective in reducing anxiety [17]. By substituting natural materials and food waste as a gelling as well as a capping agent, we can have a cleaner environment by eliminating expensive chemical compounds [20]. Gelatin is a substance obtained from the hydrolysis of bovine bones and cartilages. Gelatin components consist of 84% protein, 2% ash, and 14% moisture. Gelatin is hydrolyzed collagen [21]. It is only soluble in hot water and is insoluble in cold water, and after dissolving in water at 40 to 50 °C, it absorbs about ten times its volume of water [21]. The main constituents of gelatin are the essential amino acids, including glycine, proline, hydroxyproline, glutamic acid, alanine, arginine, and aspartic acid [21]. The existing carboxyl functional group in these amino acids can turn into carboxylate ions through exchanging electrons with the existing amine group [21]. Existing carboxylate ions can surround the metal cations, form bonds, and enter condensation reactions with other carboxylate and amine groups to form a dense gel. Then, oxide nanoparticles can be prepared through drying and heating the wet gel [22]. The main aim of the present study was the administration of synthesized zinc/iron oxide nanocomposites to an animal model of anxiety to assess if the nanoparticle can reverse the adverse anxiety behavior.

Methods: Materials The produced materials of Sigma-Aldrich, such as Iron (III) Nitrate Nonahydrate Fe(NO3)3.9H2O and Zinc acetylacetonate hydrate (Zn(C5H7O2)2.6H2O) or Zn(acac)2 and materials of Merc Co, include

methanol and chloroform, were applied in this study. Also, colorless, odorless, and essential oil-free animal (edible) gelatins were prepared from the traditional medicine market. Synthesis of zinc/ iron oxide nanocomposites (ZIONC) In the present study, a modified sol-gel method was employed for the synthesis of ZIONC. Next, Zn(acac)2 and iron nitrate were dissolved in 50 mL of deionized water in a 1:2 stoichiometric ratio and stirred magnetically for preparing a homogeneous solution. In the next step, 2g of natural animal gelatin was added to deionized water, stirred, and heated at 80°C to provide a viscous and uniform gel. The prepared metal salt solution was then added to the gel and stirred (by a mechanical stirrer) until the zinc and iron ions were uniformly distributed throughout the mentioned gel. Here, the container containing the sample was first placed at 90 °C for 24 hours for dehumidifying until a uniform, low-moisture, and faded brick red color gel was produced due to the formation of a set complex of iron ions and acetylacetonate. Then, the processed gel was placed in a muffle furnace at 550 °C for 4 hours. Since most of the gel is released as smoke, vapor, and foul-smelling gases up to about 300 °C, it is recommended that the previous step be performed under a fume hood and/ or laboratory ventilation. The obtained product was further treated (washed) with distilled water and ethanol. Next, an Ultrasonic Bath and a deionized water solvent were employed to disperse the nanoparticles and separate possible organic matter. Finally, ZIONC was dried in an oven at 75 °C for 24 hours after filtering the resulting mixture [23]. Characterization At this stage, different techniques, such as Fourier-transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), scanning electron microscope (SEM), photoluminescence spectroscopy (PL), and transmission electron microscope (TEM), were employed toward characterizing synthesized ZIONC powder. Also, the size of the synthesized crystallite was estimated using the Debye-Scherrer equation through the following formula: (1) In which: D is the crystalline size in nm scale, λ is the wavelength of the X-rays (λ= 4 1.5416), k is the equilibrium constant of the equation and depends on the particle morphology (approximately equal to 0.89), β is the full-width at half-maximum (FWHM), and θ is the Bragg angle. Injection of ZIONC At first, normal saline was applied in preparing the investigated ZIONC suspension of the present study. Then, the diluted suspension was injected intraperitoneally using insulin syringes at doses of 1.25, 2.5, and 5 mg/kg/day for 12 days. Studied animals (statistical community) and their care conditions The study population of this study included 80 outbred adult male Wistar rats (220-250 g). The studied rats were kept in conditions with an average temperature of 25 °C, the relative humidity of 55 %, and a light/dark cycle of 12:12. It should be noted that the rats had easy access to standard food and water. Sampling and sampling methods In this study, 80 male rats were divided into eight groups (n= 10 per group) as follows: 1. The control group (CO) that did not take the ZION treatment and noise stress. 2. Rat groups (Three groups) that were

treated with ZION at doses of 1.25, 2.5, and 5 mg/kg/d for 12 days while were not exposed to noise stress (CO+N1.25, CO+N2.5, and CO+N5). 3. Stress group (ST): Rats that were received normal saline and were exposed to noise stress for 12 days (from 8 AM to 12 o'clock for 2 hours). 4. Rat groups (Three groups) that were exposed to noise stress for 12 days (from 8 AM to 12 o'clock for 2 hours) and were received different doses of 1.25, 2.5, and 5 mg/kg/day at the beginning noise stress until the EPM test (ST+N1.25, ST+N2.5, and ST+N5). Noise protocol At first, the sound caused by traffic in one of the busiest squares of the Kashan city was recorded by a standard audio recorder to investigate the effects of noise stress in experimental animals. Then, its intensity was set equal to 95 decibels using sonar software (version 8.5). Next, a small speaker has placed at a distance of 30cm from the cage floor in the middle of the animal cage (a metal-reflective chamber with dimensions of 60 × 60 × 60 cm) to apply the recorded sound. Also, the sound intensity was monitored throughout the study using a sound level meter to apply noise stress with the same sound intensities according to the experimental treatments. On the other hand, although the recorded sound covered a wide range of audio frequencies, just annoying noises were considered here. Also, all study groups received sound (noise) stress at a specific hour (according to experimental treatments) every day [12]. Elevated Plus Maze Test The basis of the Elevated Plus Maze (EPM) Animal Anxiety Test (EPM) is established based on the animal searching instinct and test animal's aversion to open and bright spaces. In other words, despite the animals' tendency to move and search in all arms, they avoid entering open arms. Accordingly, a strong approach-avoidance conflict is created for animals (conflict and anxiety are created in animals) and causes animals to spend most of their time in the closed arms [24]. The EPM is a metal or wooden plus (+) shaped maze with four black arms, which has a height of 50 cm above the ground. In general, two arms of the maze are open (in dimensions of 50×10 cm), and two other arms have walls of 40 cm in height without side and end roofs with dimensions of 50×10 cm. It was also placed a square in sizes of 10×10 cm at the intersection of the four arms. At this stage, animals were placed in a box with dimensions of 50×50×35 cm before every test for five minutes to familiarize the animal with the maze and increase the animal search activities. The selected rats were then placed in the maze room at least one hour until the test time. The animals were randomly selected and were then placed one after the other (facing one of the open arms) in the middle of the maze intersection square to move freely for five minutes. Eventually, it was evaluated the number of entries into closed and open arms and time spends on arms. In general, the numbers of entry or exit of rats' hands and legs were considered as inclusion and exclusion criteria for the studied evaluations, respectively. The percentage of time spent in the open arms of the elevated plus-maze and the percentage of open arm entries for

rats was calculated using the following formulas, respectively. Where: OAT, CAT, and OAE are Open Arm Time, Closed Arm Term, and Open Arms Entries, respectively. Statistical analysis The data were analyzed by SPSS (ver 20) and Two-way analysis of variance and Post hoc Tukey's test used at $p< 0.05$ to compare the mean of the data. Ethical considerations This paper has tried to perform ethical considerations in animal experiments by the ethical considerations of the Kashan University of Medical Sciences. Accordingly, the studied animals had access to adequate food and water, and the lowest possible number of animals was also employed in this study.

Results: Investigating anxiety The results of the Two-way analysis of variance and Post hoc Tukey's test showed that sound stress had significant effects on the parameters assessed between the control and the stress groups in rats in EPM ($F_{7, 56}= 3.123$; $P< 0.001$). Besides, it was observed that injections of ZIONC doses (1.25, 2.5, and 5 mg/kg/d) caused anxiety behavior in the control group so that behavior changes of rats in this group were similar to the rats' behavior in the stress group following the receiving the studied doses of ZIONC ($P= 0.068$, $P =0.214$ and $P= 0.621$, respectively). On the other hand, data analysis showed that injection of different doses of ZIONC (1.25, 2.5, and 5 mg/kg/day) had no significant effects on improving the anxiety behavior of nanocomposite-receiving stress groups ($P= 0.187$, $P= 0.098$, and $P= 0.412$, respectively). The results of the obtained mean comparison between the application of different ZIONC doses to control and stress groups revealed that there were no significant differences in the parameters measured in the inhibitory avoidance task. The number of entries of animals into open arms is shown in Fig. 2. According to the results, it was concluded that exposure of rats to sound stress led to adverse effects on their anxious behavior. In other words, there were significant and direct correlations between the frequency of entries into the open arms between control and sound stress groups. On the other hand, it was observed that injecting doses of 1.25, 2.5, and 5 mg/kg/day of ZIONC to the examined rats in the control group resulted in the incidence of anxiety. In this regard, the injection of all three studied doses of ZIONC had no significant effects on improving the anxiety behavior of animals in the stress group receiving nanocomposite. The results of the data analysis of this experiment and the time spent of the tested animals in open arms indicated that sound stress caused anxious behaviors in rats so that the time spent of the animals in open arms in the sound stress group significantly shorter than the control group. On the other hand, although the injection of all three doses of ZIONC to the studied rats in the control group produced anxiety behavior, the injection of the mentioned doses had no significant effect on improving the behavior of rats in the stress group receiving ZIONC. Results obtained from the synthesis of ZIONC In the nanocomposite synthesis section of the present study, ZIONC was first

synthesized and characterized according to the modified sol-gel technique. The obtained XRD pattern also showed that ZIONC was formed in three phases of ZnFe2O4, Fe2O3, Fe3O4 based on the standard picklists so that the mentioned phases created different peaks in 2Θ around 30, 35, 57, and 63° (Fig. 3). The TEM image taken from ZIONC (see the colored areas in Fig. 4) indicates the formation of a two-phase structure and a two-component composite derived from iron and zinc salts. Also, the synthesized plate-structured nanocomposite is observed in a range sizes of about 20 to 60 nm. The plate-like structure of ZIONCs (synthesized by the green chemistry method) is clearly shown in the image obtained by the SEM technique. Since SEM is an analysis method to determine the morphology of particles' surface, Fig. 5 displays the contrast differences of the atomic number of the multiphase of the ZIONC, which confirms the formation of the composite structure of the synthesized product. Investigating anxiety Assessing the inhibitory avoidance behavior of animals using EPM is recognized as one of the most well-known approaches to investigate anxiety and anxiety-like behaviors in animal experiments. The statistical results of the present study confirmed that sound stress in EPM conditions had adverse effects on the anxiety behavior of treated rats so that, considering the measured parameters, significant differences were observed between the control and stress groups. In contrast, the injection of the different doses of ZIONC induced anxiety in both control and stress groups, and animals in the two groups showed the same behaviors. Statistical analysis of the data also determined that the injection of different doses of ZIONC had no significant effects on improving the anxious behavior in the noise-exposed animals. On the other hand, the data taken from the ZIONC treated animals indicated significant differences between the control and stress groups. Our findings indicated the destructive effects of sound stress on the anxiety behavior of the testing rats. Some studies have shown that reducing the intensity of acoustic waves decreased stress hormones, especially norepinephrine. Therefore, through stimulation of the hypothalamus-pituitary-adrenal axis (HPA), stress stimulates the release of the cortisol and corticosterone hormones in humans and rodents, respectively. Prolonged exposure to acoustic waves leads to physiological and psychological disorders and increased oxidative stress [25]. Ahmadi et al. (2017) found that different levels of noise stress increased the anxious behavior in the treated animals so that the number of entries into and time spent in open arms was decreased in the EPM [25]. Consistent with our results one study reported increased anxiety behavior in rats exposed to sound stress [26]. Also, the application of ZIONC in control groups resulted in increasing anxiety and decreasing the number of entries into the open arms and time spent in open arms. Torabi et al. (2015) reported that administration of 1 mg/kg of zinc oxide and zinc nano-oxide (ZnO NP) significantly reduced the anxiety behavior of rats. Also, they showed that the anti-anxiety effects of

ZnO NPs were higher than those of zinc oxide. Therefore, the anti-anxiety effects of ZnO NPs may be due to the physical and chemical properties of nanostructures and their small size, which leads to increased strength and penetration rate into the body tissues. It has also been confirmed that a high surface area to volume ratio in nanoparticles increases the availability of active-sites than the conventional compounds and can consequently have greater effects in smaller amounts than similar conventional compounds [27]. In general, it can be stated that zinc ions are involved in the stimulation and activity of several enzymes in the body and affect receptors of numerous neurotransmitters such as GABA, Serotonin, NMDA, and voltage-gated calcium channel [28]. These receptors can also play principal roles in the modulation of anxiety. Besides, since zinc ion is an essential element for the physiological function of the brain and other organs [29], the use of organic and inorganic supplements containing zinc can partially improve anxiety in animal models [30]. Despite the limited information on the mechanism of the anxiolytic effects of ZnO NPs, it has been suggested that zinc ions released from nanocomposites may have anxiolytic effects in animals via at least two mechanisms [28]. First, some studies have shown that zinc ions regulate glutamate signaling by inhibiting NMDA receptors. In general, zinc ions and glutamate are released together in the presynaptic space. Glutamate is one of the most important excitatory neurotransmitters in the modulation of anxiety-like behaviors. Zinc ions impair glutamate function in anxiety by inhibiting the most well-known glutamate receptor or NMDA receptor. Second, zinc ion acts as an inhibitory neurotransmitter reducing glutamate presynaptic output, decreasing glutamate signaling, and subsequently preventing the anxiety occurrence through increasing GABA presynaptic output [31]. Khajehpour et al. (2019) reported that despite the additive effects of intraperitoneal injection of ZnO NPs, with Fe_2O_3 phase, under a dose of 7.5 mg/kg on the anxiety behavior of adult male rats, it was observed no significant effects on changing the anxiety behaviors of rats treated with a concentration of 5 mg/kg of ZnO NPs. They attributed the results to iron deficiency, especially in the dorsal hippocampus, which may induce increased anxiety-like behaviors in animals. It has also been suggested that high levels of iron in the brain can lead to decreased brain function, increased neuronal death, and impaired production and release of neurotransmitters including acetylcholine, adrenaline, and serotonin. Also, abnormal functioning of these systems can cause increased anxiety behaviors [31]. Kesmati and Khorshidi (2013) also found that intraperitoneal injection of 0.2 mg/kg of Fe_2O_3 nanoparticles into rats had no notable effects on animal anxiety behaviors while injections of 2 and 5 mg/kg reduced the anxious behaviors of the studied animals. Their results were due to the anti-anxiety properties of Fe_2O_3 nanoparticles at doses of 2 and 5 mg/kg [16]. Different researches focus on iron oxide nanoparticles. In one study, intraperitoneal injection of Fe_2O_3 nanoparticle with a concentration of

more than 7 mg/kg had synergistic effects on anxiety behavior while application of 5 mg/kg level had no significant influences on this parameter. On the other hand, doses of 2 and 5 mg/kg of Fe2O3 had anti-anxiety effects in another study. In general, in previous studies, iron seems to be functional in the ferric (Fe3+) state, but the ferrous (Fe2+) state is present in a part of the stoichiometry of the preparation of ZIONC. Intraperitoneal injection of ZIONC helps zinc ions to transmit through the bloodstream to other organs of the body. Also, due to the presence of the ferrous state of the iron element in red blood cells, the increase in Fe2+ levels in the blood can appear via the ionic transport of the synthesized ZIONC. According to a study by Eseh and Zimmerberg (2005), iron deficiency leads to an increase in anxiety behavior in female rats [32]. Hence, it can be concluded that increasing the amount of Fe2+ state leads to improved anxiety behavior in animals. On the other hand, since serotonin plays critical roles in mediating emotional behaviors in the brain, iron deficiency causes changes in the serotonergic system that lead to the incidence of anxious behaviors. However, the effect of iron deficiency in the dopaminergic system is more durable and prevalent (which has both effects on increasing anxiety and changing motor activity). More than anything, chronic (long-term) iron overload can also damage a wide range of body tissues, including beta cells in the liver, heart, and brain. Iron accumulation increases the incidence of diastolic and systolic heart failures, which in turn impairs cardiac function, increases oxidative stress, and Intensify anxiety. On the other hand, iron overload can lead to an increase in reactive oxygen species (ROS), disrupt in the function of antioxidant (AO) defense systems, and consequently increase oxidative stresses. Despite many studies in this field, there is no proven mechanism on how iron-overload affects and disrupts the antioxidant systems. High levels or deficiency of iron seems to affect oxidation and reduction mechanisms and affect the occurrence of anxiety behaviors through affecting the antioxidant defense systems and changes in the concentration of the produced oxidants. In general, it is proven that disturbances in iron concentrations in various brain regions, including the hippocampus, create significant effects on the occurrence and development of anxiety behaviors [33], which is consistent with the observed effects of ZIONC on anxiety-like behaviors in the present study. Because of the highest concentrations of iron in brain regions, such as dopaminergic structures, the indirect effects of iron on anxiety and pain behaviors mediated have been investigated by the dopaminergic system in some studies [34]. It has also been reported that iron deficiency-induced in the rats' diet leads to a decrease in dopaminergic receptors [35] [25, 26]. Besides, anxiety-like behaviors were found to be associated with density and dopamine receptor D2 in the prefrontal cortex. Accordingly, the iron has a direct role in the synthesis and binding of dopamine receptor D2, and its reduction can reduce dopamine receptors in the striatum and midbrain [26].

Given the above, the iron released from ZIONC may exert a part of its anti-anxiety effect through the dopamine system. On the other hand, identifying systems or mechanisms that mediate this process requires more detailed future studies. Synthesis of ZIONC In general, the obtained results of the XRD analysis showed that the intensity of the peaks of the synthesized ZIONC was lower than the peak intensity for the bulk state analysis. The expanding of the base of the peaks indicates nanoscale structures for the synthesized ZIONC. The size of the synthesized crystallite was estimated equal to 20 nm using the Debye-Scherrer equation. Also, a comparison of the obtained XRD pattern with standard picklists and previous works for different pattern peaks in 2Θs around 30, 35, 42, and 58° showed that ZIONC was formed in the ZnFe2O4 phase [36]. Here, the characterization of the synthesized ZIONC surface was detected using SEM images [5]. ZIONC disk and plate structures are clearly defined in the obtained SEM images. According to the obtained a, b, c, and d regions in Fig. 4 and the contrast of the atomic number (Z-contrast), it can be observed that the brightest and darkest phases indicated the highest and lowest atomic numbers, respectively. Hence, the above results confirm the multiphase structure of the XRD pattern. According to the nanostructured synthesis technique and raw materials used in the present study, a maximum of four phases ZnFe2O4, Fe3O4, Fe2O3, and ZnO were identified with molecular masses of 241, 231, and 159 g/mol. On the other hand, it was found that regions α and b are closer to the ZnFe2O4 phase through examining the XRD pattern and the proximity of the molar masses of the two phases of ZnFe2O4 and Fe3O4 with the numbers of 241 and 231. Besides, regions c and d may correspond to the Fe2O3 and ZnO phases. Therefore, according to the above evidence, it can be recognized that the powder synthesized by the modified cell-gel technique is a multiphase nanocomposite consisting of zinc and iron oxides. TEM images are a well-known analysis in determining the structure of nanocomposites. The amalgamation of different phases of nanocomposite formations, as a primary condition of a nanostructure formation, is detected by the electron beam passage from the structure of nanoparticles and nanopowders. The results in Fig. 4 (Atomic Number Contrast Technique) showed that at least two mixed phases were formed in regions α and b. The standard sol-gel process is a wet-chemical technique that uses solvents, such as ethanol and molecular precursors (usually metal alkoxide), toward synthesizing various types of nanostructures, especially metal oxide nanoparticles. In this study, natural gelatin was applied as a gelling and coating agent. Also, water was used as a solvent, and simple mineral salts were used as precursors by removing expensive precursors of the Alkoxy group and alcohol solvent. Therefore, the production of wastage in this method is reduced, which is known as an indicator in green chemistry and environmentally friendly chemical reactions, and less damage to the environment. Also, the speed of the process of converting sol to gel and, thus,

the compaction speed of gel encourage using this method. Laser Ablation Nanofilms technique is a proper method in the synthesis of different composites of zinc and iron oxides [37]. Also, it is shown that Fe-ZnO nanocomposites are prepared using metal nitrate precursors by the application of coprecipitation and sonochemical methods [38, 39]. Besides, the Fe3O4/ C/ ZnO three-component nanocomposite was obtained in some studies by a one-step sol-gel process, in which lignin amine (LA) was utilized as the carbon source and ligand donor agent [39]. Various mixtures of oxide nanocomposites, such as Fe2O3/ZnFe2O4, Fe2O3/ZnFe2O4/ZnO, and ZnFe2O4/Zn, were formed by a hydrothermal method via changing the molar ratios of iron and zinc salts and then calcination at 500 °C [40]. In some studies, the coprecipitation technique was also employed to synthesize ZIONC using natural animal gelatin (pig skin gelatin) as a capping and ligand donor agent [41].

Conclusion: CONCLUSION Sound stress profoundly affects anxiety and anxiety-like behaviors. The results of the present study showed that the intraperitoneal injection of ZIONC in sound stress rats reduced anxiety-like behaviors. Also, the modified sol-gel (MSG) method and using gelatin in ZIONC synthesis led to the production of plate-structured nanocomposites. ACKNOWLEDGMENT This study was supported by Islamic Azad University Shahrekord Branch, Iran and Kashan University of Medical Sciences, Iran. Thanks are due to Dr. Mokhtar Panahi-Kalamuei from Institute of Nanoscience and Nanotechnology, University of Kashan, Iran for their laboratory supports. CONFLICT OF INTEREST The authors declare that there is no conflict of interests regarding the publication of this manuscript.

Keywords: Zinc/Iron oxide nanocomposites, anxiety, noise stress, elevated plus maze

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Zoonotic Transmission of Cryptosporidium: A systematic review and Future Directions (Review)

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Introduction: A wide range of hosts can be infected by Cryptosporidium species, enteric parasites that are found all over the world and have a wide distribution. Viral-oral transmission occurs through contaminated water, food, or direct contact with humans and animals. Although first described in 1907 by Tyzzer , Cryptosporidium did not come to prominence until the early 1980s. This is when it was identified as a cause of severe and protracted diarrhea and death in HIV+/AIDS patients. It is now recognised as a major pathogen in children and immunocompromised adults and after rotavirus is the most serious diarrheal pathogen in young children . There was a large waterborne outbreak of Cryptosporidium in Milwaukee in 1993 that affected over 400,000 residents. Though it is under-reported, Cryptosporidium is a well-known and major cause of gastroenteritis outbreaks both in the water and in food. Among the reasons for this are the resistance of the environmental stage, the oocyst, to disinfectants, such as chlorine treatments in drinking and recreational water. Several Cryptosporidium species from mammals and birds, such as C. parvum, C. meleagridis, C. canis, C. felis, and C. ubiquitum, are significant zoonotic pathogens, causing animal contact-associated or waterborne and foodborne cryptosporidiosis in humans.Although six common species are identified in humans, including C. hominis and C. parvum.This review aims to summarise the currently available data on zoonotic transmission of Cryptosporidium species and genotypes. It also outlines future studies required to better understand this ubiquitous parasite's transmission dynamics.

Methods: Four global databases (PubMed, Web of Science, Scopus and Google scholar) were searched. The searching process was accomplished using MeSH terms alone or in combination: (“Coccidian” OR “Opportunistic protozoa” OR “Cryptosporidium” OR “Cryptosporidiosis”) AND (“Prevalence” OR “Epidemiology”) AND (“humen” OR “zoonotic”) ,6200 studies funded. After removing duplicates and excluding ineligible reports, 127 articles, containing 160 datasets, were eligible to be included in this systematic review .42 relevent articles with complete abstracts were included in the study.

Results: Cryptosporidium species are widespread enteric parasites with diverse hosts, primarily transmitted through the fecal-oral route via contaminated water, food, or contact with humans and animals. Initially described in 1907, Cryptosporidium gained prominence in the 1980s as a cause of severe diarrhea and mortality in HIV/AIDS patients. It is now recognized as a significant pathogen in children and immunocompromised individuals, ranking as the second most common cause of diarrhea in young children after rotavirus. Cryptosporidium is notorious for causing both waterborne and foodborne gastroenteritis outbreaks, as its oocysts are resistant to disinfectants. Various Cryptosporidium species, including C. parvum and C. meleagridis, are zoonotic, posing risks to humans through animal contact, waterborne transmission, or contaminated food. The parasite has a complex life cycle involving ingestion and excystation of oocysts, leading to infectious thick-walled oocyst shedding in feces. In humans, cryptosporidiosis can lead to watery diarrhea, abdominal pain, vomiting, malnutrition, cognitive deficits, and even colon cancer. While typically self-limiting in healthy individuals, it can become chronic, particularly in immunocompromised hosts, and neonatal livestock may experience severe diarrhea and death. At the moment, the only FDA-approved drug, nitazoxanide, is also widely ineffective and while Halocur® (halofuginone lactate) is available in some countries as a prophylactic, its effectiveness is variable, and it cannot be given to animals already suffering from diarrhea. In addition, there is no approved vaccine. Due to Cryptosporidium species' morphological similarity, 18S ribosomal RNA typing is crucial for identification. C hominis and C parvum are the most important human genotypes among 44 species and >120 genotypes. Cryptosporidiosis epidemiology is heavily influenced by zoonotic transmission. Waterborne outbreaks are a global concern, with reports from various countries.

Conclusion: Cryptosporidium, a globally distributed enteric parasite, poses a significant public health concern due to its wide host range and transmission through contaminated water, food, and direct contact. Cryptosporidium's resilience, notably the resistance of its environmental stage, the oocyst, to disinfectants, contributes to its persistence and its role as a major cause of gastroenteritis outbreaks. Several Cryptosporidium species from mammals and birds are significant zoonotic pathogens, with zoonotic transmission not fully understood in some cases. Future research is needed to enhance our understanding of the transmission dynamics of this ubiquitous parasite

Keywords: Cryptosporidium, parasite , zoonosis