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1. **3D reduced graphene oxide fabrication for repairing neural tissue (Research Paper)**

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Introduction: ECM plays ansubstantial role in cell setting behaviors by influencing on cells through biochemical messages and topography factors and adjusts hemostasis (balance) of the cell. Reconstruction of the spinal cord and improvement of the function of the isolated neural tissue requires an extracellular matrix to guide the neural cells and the absence of this matrix is the major limiting factor. In vivo, cells are enclosed in three-dimensional microstructures. These structures named extracellular matrix (ECM) are composed of collagen and regulate cells, elastin, and laminin, at the nanoscale level each having its specific bioactive role. ECM plays a considerable role in regulating cell behaviors. In fact, it affects cells through biochemical messages and topographic factors and regulates their homeostasis. In vivo conditioned cells are in a three-dimensional environment and compared to two-dimensional culture, they exhibit different morphology and phenotypic characteristics. Consideringly, a structure similar to the ECM could provide a more suitable environment for directing cells in migration, adhesion and proliferation functions. A 3D model can provide a better sense of the phenomenon occurring in vivo under laboratory conditions. In this space, graphene can be a good substance for scaffolding with the ability of discerning stem cells from neural ones. Recently, graphene and its derivatives have been utilized as constituents of several carbon-based substances including 1D tube-in-tube nanostructures, 2D layer stacked films, and three-dimensional hydrogels [1-4]. Graphene, as one of the carbon allotropes, has different properties than other allotropes or carbon-based compounds e.g. benzene. As a result of these unique properties, the application of graphene in tissue engineering has certain advantages. Its substantial features as low molecular weight, elasticity, electrical conductivity, and adsorption of protein may change the orientation of stem cell differentiation and neural cell proliferation. Another important feature of graphene that is remarkable in tissue engineering is its ability to absorb protein and low molecular weight chemicals. By secreting various substances, cells can grow or communicate with neighboring cells. These materials, after adsorption onto graphene, contribute to cell proliferation and differentiation. Adsorption of lightweight molecules and proteins on the graphene surface occurs through ionic bonding and hydrophobic interactions between nerve and stem cells cultured on graphene [5-6]. Materials involved in nerve cell guidance must be able to physically support axonal development and not be toxic or irritating. They should also be viably able to modify and improve the loading site of molecules promoting growth and guidance [7-8].The effects of graphene oxide aerogel (GOA) when applied to neural cells on their behavior and differentiation will be discussed in detail. Then, the results of cytotoxicity studies on GOA will be presented.

Methods: Experimental section Materials and methods Ethylenediamine, natural graphite, and H2SO4 (97%) were purchased from Merck (Darmstadt, Hesse, Germany). KMnO4 (99%), and H2O2 (30%) were provided from Sigma- Aldrich (Saint Louis, MO, USA). Mouse fibroblast cells (L-929) and P19 cells from Genetic Institute of Iran. To get the required material of Trypsin-EDTA, DMEM-F1 (Dulbecco's Modified Eagle's Medium) solution and fetal bovine serum (FBS), we bought them from Gibco BRL laboratories, Germany. Synthesis of graphen oxide (GO) Graphene oxide (GO) was produced according to Hummer's method. In this chemical process, natural graphite (1g) was mixed with H2SO4 (50 mL) in a pyrex reactor with a volume of 10 L. The reactor was fitted with a water cooling system. The mixture was stirred at a rate of 400 rpm for a duration time of 10 min. Afterward, KMnO4 (6 g) was gradually poured on the content of the reactor within 60 min and the prepared mixture was agitated for a duration time of 120 min at a rate of 800 rpm and room temperature. In the following step, using an amount of D.I. water (100 mL, GFL, Germany), the generated suspension was diluted. After that, some amount of D.I. water (200 mL) and H2O2 (6 mL) were poured on the mixture to remove excess metal reactants and ions from the mixture. Consequently, the reaction mixture color was altered from green-brown to a brownish-yellow. Then, through centrifuging at a rate of 6000 rpm for a duration time of 60 min which repeated 4 times, non-target materials such as salts and acids were separated. This step was applied by SIGMA 3-18K Centrifuge.The resultant centrifuge top solution then exposed to the ultrasonic waves for a duration time of 30 min. For this step, an ultrasonic bath of Elmasonic was used which adjusted at a frequency of 40 kHz and a power of 150 W. subsequently, the obtained transparent stable aqueous suspension of GO was centrifuged at a higher rate of 2000 rpm for a duration time of 15 min. As the ultimate step, GO suspension was filtered using ashless filter paper circles and the prepared material was placed in a vacuum oven at a temperature of 70 °C for a duration time of 24 hours to be dried [9-11]. Highly porous 3D GO synthesis According to the conventional method [12-13], a homogenous mixture is first made of GO and ethylenediamine and then the mixture is placed in a glass vial and sealed. The glass vial is heated for 6 hours at a temperature of 90 ° C. This process is aimed at the hydrogel synthesis from functionalized graphene. After the reaction is complete, the process product is washed with a large amount of water to remove the GO that has not entered the hydrogel network. Also, to ensure the withdrawal of non-reacted ethylene diamine, the prepared hydrogel was washed with double distilled water every four hours. This washing process was continued for 48 hours. Finally, the washed hydrogel was placed in a freeze dryer for 24 hours. FTIR In the present study, to detect the bonding and chemical structure of GOA, FTIR spectroscopy of the NEXUS 870 Thermo Nicolet company in the United States was used. Scanning Electron Microscopy (SEM) The SEM images were captured using the scanning electron microscope (Seron Technology, AIS-2100, Korea), and these examinations were carried out at the room temperature. Before imaging, samples weresputter coated with gold in order to have conductive surfaces. They were coated with Au for 10 min prior to the measurement. X-Ray Diffraction (XRD) To determine the crystallization percentage of GO and produced GOA and comparing them with each other as well as comparison of crystallization percentage of aerogel, the X-ray diffraction spectrum was used. For this purpose, the machine made by model EQUINOX3000 Inelcompany, from German country, was used and the samples

were checked by the use of X-ray at 40 KW and 30 mA, and 900 Watts. The range of angles studied was 5 to 30 degrees. MTT Assay For the cytotoxicity test of the MTT, we selected the L929 mouse fibroblast cells. First, a general examination was performed on the cells to ensure their proper condition. This task was carried out via observing the cell count, the morphologic structure of the flask containing the cell, and culture medium. In this study, the principal requirement was the viability of the L929 cells based on the standard number ISO10935. In order to sterilize the samples, they were first exposed to UV rays. Cell concentration was adjusted to 1×105 cell/ml. Moreover. Placement of the scaffolds was in a triplicate in 24 well plates, and 1 ml of cell suspension was added to each well. Since a total of 3 wells were designated for the control group, they did not receive any scaffolds. The incubation of the samples was carried out with 5% CO2 in the atmosphere and at 37°C. The incubation cell was washed after 24 hours using a PBS solution. Moreover, 100µl of MTT solution (i.e. 5 mg/ml) was added to each well and another 4 hours of incubation were followed after this addition. Fibroblast culture During some in vitro cell culture trials, the reaction between the cell culture and the scaffold was examined. L929 mouse fibroblasts were utilized in this investigation and cultured in RPMI containing penicillin (100 µg/mL), fetal calf serum (10%) and streptomycin (100 µg/mL). Before seeding, a suspension of 1.8 ×105 cells/mL was supplied. Before culturing the cell, two specimens were provided for each scaffold sample by sterilizing in ethanol (70%) and washing in the culture media. The samples were put on a plate of multiwall polystyrene accompanying the cell suspension (5 mL) and maintained in a CO2-controlled incubator with a temperature set at 37°C for 48 ± 1 hours. As a negative control, one of the samples was held on. At the end of the incubation period, all of the samples were washed with the phosphate-buffered solution of saline. Exploiting glutaraldehyde 2.5%, the cells were fixed and finally were dehydrated utilizing graded ethanol as 60%, 70%, 80%, and 95%. Culture of P19 cells P19 cell line from mouse (C422) was supplied from Genetic Institute of Iran. In order to gain a density of 5×104 cell/ml, the cells were cultured and preserved in accordance to Rudnicki and McBurney[14]. Then the cells were separated mechanically from the culture dishes and laminated into 100-mm bacteriological grade Petri dishes comprising a medium of α-MEM. This medium was supplemented with 0.3 µM retinoic acid (RA) and 10% calf serum to prompt neural P19 cells differentiation and growth as aggregates. After an incubation time of 4 days, a volume of cell suspension (1 ml) with the concentration of 5×104 cell/ml was seeded in 24 well tissue culture plate from polystyrene comprising scaffolds which cultured in a medium at a temperature of 37°C, without RA and containing CO2 (5%) and environmental humidity (95%) for a duration of 10 days. Before than cultivation, exposing to UV radiation for a duration time of 120 min, the scaffolds were sterilized and subsequently washed 3 turns with sterile PBS. Each of these washing steps lasted 20 min. Gently evacuating the medium and removing dead cells through washing the scaffolds for a duration time of 5 min led to the stabilized grown cells. Aiming the cell fixation, glutaraldehyde solution (2.5 V/V%) was subjoined to every well. Plates were kept at room temperature for a duration time of 120 min.Within 5 min, the samples were washed using phosphate-buffered saline (PBS) and dehydrated by immersion in a sequence of ethanol solutions of varying concentrations as 50, 60, 70, 80, 90, 100 v/s%. The immersion time in each ethanol solution was 5 min. Afterthat, the samples were washed again the solution of with phosphate-buffered saline (PBS) for 5 min. After eliminating

PBS, the scaffolds were completely dried at room temperature for 24 hours [15].The surfaces of tissue culture plastic was considered as the negative control. Light microscopy imaging were performed by T-FL optical microscope (Nicon model, manufactured in Japan) to examine the murine P19 cells differentiation in the matrix of scaffolds. All of the biological experiments were repeated at least three times. DAPI and immunofluorescence stainings Using DAPI (4-6-diamidino-2-phenylindole) as a blue fluorescent probe, the nuclei of cells were stained. DAPI can bind with DNA of fixed live cells which lead to specific fluorescent complexes with very high intensities. Cell staining were carried out through the following steps: washing the scaffolds with PBS for 5min; applying DAPI solution with the concentration of 1:1000; washing the scaffolds three times with PBS. Each washing step lasted 5 min. Cells labeled with this antibody and nuclei stained were examine using optical microscope and their images were captured. . Generally, the existence of cells on the scaffold can be evidenced through this method. In addition, in order to confirm the differentiation of P19 cells on the scaffolds, immunofluorescence staining we carried out. After a week of seeding the cells, the samples were translocated to gelatin-coated dishes and using a solution of paraformaldehyde (4%) in PBS for 30 min they were fixed at room temperature. The specimens were washed in PBS three times. Each of these washing steps lasted for 5 min each. With the aim of obtaining more permeability, the cells were exposed for 45 min to Triton-X (1%) diluted in PBS. Afterthat, the cells were blocked using fetal bovine serum (FBS) (5%) in PBS for 5 hours. Followingly, the samples were incubated overnight with MAP-2 (Microtubule associated protein-2) antibody (1:100) at the temperature of 4°C. The mentioned protein is a particular protein existing in neural cells. Subsequently the cells were washed using PBS three times which any of washing turns lasted for 5 min [16].

Results: Results and discussion FTIR Fig. 1 shows the absorption peaks originated from oxide groups localized on GO. The peaks appeared in 3443 cm-1 is related to flexural (bending) vibrations of O-H group; in 1746 cm-1 belongs to tensile vibrations of C=O groups in carbonyl and carboxyls; in 1638 cm-1 reveals tensile vibrations of aromatic carbon C=C; in 1236 cm-1 indicates tensile vibrations of the carboxyl group of C-O existing in –COOH; in 1071 cm-1 denotes the tensile vibrations of epoxy groups (1 and -2 ether), and finally the peak appeared in the wavenumber of 665 cm-1 is attributed to the change in the form of the C-H group attached to C = C. The presence of these functional groups causes the GO polarization, which justifies the ease of homogeneous distribution in the water. Fig. 1 shows the FT-IR spectra of GOA (Run 15). Moreover, a slight intensificationof the peak at 1089 cm−1 was also observed after ethylenediamine grafting on GOA. After GO reduction by ethylenediamine, a significant decline occurred in the intensities of the peaks rised from the oxygenated functional groups. For example, the peak of –OH deformation vibration appeared at 3427 cm-1 shows this tendency. The new peaks appeared in the region of 1568 cm-1 and 1160 cm-1 is assigned to the strong in-plane C–N scissoring absorption and C–O stretching vibration, respectively [17-19]. Fig. 1 FTIR spectrum of graphite, GO, and aerogel GO Scanning electron microscopy (SEM) Fig. 2 shows the SEM images of GOA (graphene oxide aerogel) sheets. Obviously, a honeycomb-like cellular structure can be seen. The cell walls are composed from assembled graphene sheets produced through the freezing step. At this step, the individual sheets are pressed

together to form ice crystals. The in-plane size of these integrated sheets can be up to several tens of micrometers. leading to an enhanced elastic stiffness. This assembling is led to a well-defined and interconnected 3D porous network with increased elastic stiffness. Fig. 2 SEM images of the cellular structure of GOA shown in (a) and (b) X-Ray Diffraction (XRD) Fig. 3 shows the X-ray diffraction patterns of graphite, GO and GOA. According to literature, the natural graphite displays a basal reflection peak (002) at 2θ =27.168° with a d-spacing value of 3.282 °A [20]. However, after oxidation, the mentioned (002) reflection peak was shifted to 2θ =11.148° with a d-spacing value of 7.936 °A. This shift indicates the intercalation of oxygen functional groups to the graphite basal plane [21]. In the XRD pattern of GOA, a new wide peak appears at 2θ=23.9 (d-spacing 3.717 °A) indicating GO sheets reduction and the separation of sheets accompanying EDA attached to them [13]. These results propose the role-playing of π-π stacking between the graphene sheets in the graphene aerogel and the inhomogenous graphite-like carbon crystalline state [22]. Fig. 3 X-ray diffraction patterns of GO, GOA, and graphite 3.3. MTT Assay The results from the MTT test on scaffolds following 48 hours of culturing of the cells are demonstrated in Fig. 4. In specific, the cell's survival ratio on the scaffolds was measured using the formazan absorption rate. The cell's growth ratio can be seen at 570um wavelength in the diagrams illustrated. Cell viability of 100% is a standard value for the nontoxicity of the biomaterial samples. All the samples produced in this study were biocompatible after 48 hours. This biocompatibility implies a lack of toxicity in L-929. The scaffold's cell viability and the L-929 cell contact were 118%. Fig. 4 MTT assay of a scaffold Cell culture The SEM images clearly display the overall structure, interaction, and adhesion of cells to the samples. The interconnection between cells is well demonstrated in the scaffold image. It is more difficult to take appropriate images in the scaffolds due to their porous structure and the penetration of cells therein. Fig. 5 shows the penetration of cells into the porous structure. It should be noted that it is difficult to distinguish the cells from the surface roughness due to the nonuniform scaffold surface. Nonetheless, high-quality images were reported herein. Fig. 5 SEM images of GOA along with the fibroblast culture after 48 hours (a) and (b), SEM images captured from the cross-section of GOA by fibroblast culture after 48 hours (c) and (d). Culture and Differentiation of P19 Cells SEM images were examined which are shown in Fig. 6 These images can demonstrate the interaction between scaffolds and differentiated P19 cells after 14 days of cell culture. According to these studies, it can be said that the neurons of embryonic stem cells (ESCs) can be differentiated on the support of structures having suitable biological and chemical behavior. Thanks to their ability for differentiation into neuronal groups, ESCs can be utilized on scaffolds to restore neural damage. This study demonstrates that the scaffold synthesized in the proximity of differentiation factors could be a better substrate for ESCs neural differentiation. However more explicit tests and functional investigations need to be performed to prove these findings. The results of these experiments demonstrate that the designed scaffold may facilitate ESCs differentiation into more effective neurons. Fig.6 SEM images (a and b in two different magnifications) of the interaction between P19 murine cells and scaffolds after 14 days of culture. Immunofluorescenc Fig. 7 and Fig. 8 show that the cells marked with MAP-2 antibodies could be observed under a microscope. Bright green phosphorus areas show a positive reaction against their specific antibodies due to the presence of MAP-2 proteins, which were observed

and recorded by the microscope. The presence of this protein, specific to neuronal cells, proves that P19 cells were successfully differentiated into neurons after the cell culture process. Fig. 8 illustrates the cell differentiation into the scaffold by immunochemical staining technique for neuron-specific protein marker as MAP-2 (microtubule-associated protein 2) antibody. Cells were fixed in different development stages and stained using anti-MAP-2. The morphology of the cells stained with this antibody is shown in Fig. 8. It confirms the differentiation of P19 cells into neuron cells. At the end of 14 days cultivation, the staining of MAP-2 was acquirable on the surface of the scaffold. The cells on the scaffolds were extremely immunopositive for MAP-2. In our study, we have shown that GO scaffold is a proper choice for P19 cell adhesion and differentiation to neural cells. In Figs. 7 and 8, the green phosphor dots are the points with a positive response due to the presence of MAP-2 protein against its special antibody. This confirms that P19 cells of mice in the course of the cell culture steps have been differentiated well into neural cells. Alongside the positive response of cells to the staining, the intensity of this reaction is also considerable. Considering the large count of green dots in the images of immunofluorescence staining, it can be said that a large number of murine P19 cells can be differentiated into the nerve cells. More interestingly, since cell differentiation was about 16% on the control surface and about 89% on the scaffold surface, P19 cells were effectively differentiated into neural cells, indicating the effective role of GOA in neuronal differentiation. Fig.7 Fluorescence imaging of the cells marked with Map-2 antibody on the negative control after 14 days of culturing, (a) nuclei stained by DAPI, (b) primary antibody to MAP2, (c) merge, magnification:400×, Positive reaction: 16.4%. Fig.8 Fluorescence imaging of the cells marked with Map-2 antibody on the scaffold after 14 days of culturing, (a) nuclei stained by DAPI, (b) primary antibody to MAP2, (c) merge, magnification:400×, Positive reaction: 89.5%. More interestingly, the cell differentiation rates of ~16% and ~89% respectively on the control and the scaffold surfaces, P19 cells were effectively differentiated into neural cells, indicating the effective role of GOA in neuronal differentiation.

Conclusion: Conclusions In this study, sample was assessed considering the physical, morphological, and mechanical characteristics as well as the cultivation of L-929 fibroblast cells and differentiation of P19 cells. Morphological examination using images of the scaffolds captured by a scanning electron microscope (SEM), disclosed the three-dimensional (3D) structure which has a lot of pores prior to mounting cells on. Based on dynamic-mechanical thermal analysis (DMTA) data, the prepared scaffold has a great storage modulus. L-929 fibroblast cells were utilized to evaluate the appropriateness of the scaffold and its cellular interaction. It was demonstrated that P19 cells could be differentiated on the surface of the scaffold. In a duration of 14 days, a highly viable, congruent, and interconnected neural network was built through a biocompatible route on the scaffolds. Further studies should be performed on the control of P19 cell growth as well as predicting the potential of utilizing these substances in neuronal repairing with the aim of evaluating the architecture and roughness and consequently the compatibility of these scaffolds.

Keywords: Neural tissue engineering., Graphene oxide, Aerogel, Hydrogel.

A bioinformatics analysis of potential differentially regulated biomarkers in hepatocellular carcinoma (HCC) related gene COL4A1 (Research Paper)

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Introduction: Hepatocellular carcinoma (HCC), one of the top ranked occurring cancers worldwide, could emerge because of hereditary background related metabolic diseases, cirrhosis, chronic hepatitis B and C (HBV and HCV) and viral infection. They lead to heterogeneous tumors diverging from different molecular factors and pathways, requiring vast inquiry for early diagnosis, biomarker detection and disease progress route and treatment; therefore, with bioinformatics and and in silico studies, precise mechanism and development of HCC, which still is unclear, could be identified. In this study, biological biomarker including micoRNAs (miRs) and long non-coding RNAs (lncRNAs) related to one of the top HCC associated pathways and significantly differential expressed genes from the collagen family, collagen type IV alpha 1(COL4A1), were perused.

Methods: The process began with selection and then analysis of GSE102079's extracted data form the Gene Expression Omnibus (GEO) with GEO2R for differentially expressed genes' (DEGs) purpose. Afterwards, functional-related gene groups with the same regulations and their related pathways, were enriched and analyzed by Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) in DAVID database. protein-protein interaction (PPI) network, for further evaluation, was erected using STRING. For miR seed matching, potential SNPs with zero distance of COL4A1 was applied in mirdSNP. LncBase v.2 was used in purpose of appropriate lncRNAs selection. At last, NONCODE was used for lncRNAs expression evaluation in both liver and HEPG2 cell lines.

Results: One has-mir-205 was elected and ten lncRNAs were identified as a competitor for both 3p and 5p has-mir-205. For has-mir-205-5p NONHSAT077300.2, NONHSAT017523.2, NONHSAT142243.2, NONHSAT021488.2, NONHSAT041650.2 and NONHSAT058723.2 were identified. As for has-mir-205-3p NONHSAT192799.1, NONHSAT017523.2, NONHSAT192676.1 and NONHSAT041374.2 were recognized. Both has-mir-205-3p and has-mir-5p were downregulated in HCC in contrast with all the lncRNAs, except for NONHSAT041374.2, which were upregulated. NONHSAT017523.2 was common in two miRs and the other notable things are presence of NONHSAT021488.2 only in liver and significant and specific upregulation in HepG2 cell lines. To note that all lncRNAs, showed differentiation in both liver expression and HEPG2 cell lines' expression.

Conclusion: Other studies show that COL4A1 is oncogene with the most upregulation out of 44 members of collagen family, which facilitates metastasis, causes more cell growth and leads to an advanced liver cancer. A competing endogenous RNAs network with mRNA, a lncRNA-miR-mRNA network, could affect drug resistance and cancer progress. miRs and possibly lncRNAs, will make fine biomarkers for a better diagnosis. With these interpretations, we suggest that has-mir-205 is a tumor suppressor and nine out of ten lncRNAs are probably onco-lncs (NONHSAT041374.2 is probably tumor suppressor. The common NONHSAT017523.2, would be a good biomarker for detecting more than one type of miRs (has-mir-205-3p and has-mir-205-5p). We also note that NONHSAT021488.2 is potentially a remarkable biomarker, because of its only and specific expression in liver.

Keywords: Hepatocellular carcinoma, microRNA, lncRNA, bioinformatics, COL4A1

A bioinformatics analysis of potential sifted biomarkers related to COL1A1 in Hepatocellular carcinoma (HCC) (Research Paper)

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Introduction: Hepatocellular carcinoma, the most commonly occurred liver cancer and froth fatal cancer globally has different risk factors including hepatitis B and C viral infection, cirrhosis, hereditary metabolic diseases and alcoholism. The precise molecular progress and tumor development is still not clear; therefore, bioinformatics analysis and related studies with HCC related gene, gene coded protein interactions, gene coding mRNAs, microRNAs(miRs) and long noncoding RNAs (lncRNAs) could suggest probable novel biomarkers leading to an early stage diagnosis and treatment.

Methods: By the help of bioinformatics database and in silico studies, after the extraction of genomic expression in both tumor and normal liver tissue and then analyzing it, one genes were selected by pathway recognition and at last, two microRNAs (miRs) along with their four competitor long non-codding RNAs (lncRNA), were sifted and studied for oncogene and tumor suppressor function identification. The route began with selection and analysis of GSE102079 form the Gene Expression Omnibus (GEO) with GEO2R for differentially expressed genes' (DEGs) selection and identification. Enriched functional-related gene groups and related pathways, were analyzed by Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) in DAVID database. protein-protein interaction network (PPIN), was constructed using STRING. As for miR seed matching, potential SNPs of COL1A1, were applied in mirdSNP. LncBase v.2 was used in order to select appropriate lncRNAs, and NONCODE for expression evaluation in liver and HEPG2 cell lines.

Results: From the suggested biological pathways, contributed genetic related factors in HCC and elected COL1A1, were obtained. Two miRs including has-mir-29a and has-mir-129 were selected with a zero distanced SNP. A total of 3 different miR related lncRNAs, were identified which showed different expression rate in both liver and HEPG2 cell lines. has-mir-129-5p includes two related lncRNAs, NONHSAT075477.2 and NONHSAT017523.2. has-mir-29a-5p's competitor is NONHSAT017523.2 and has-mir-29a-3p's is NONHSAT017474.2. In HCC, has-mir-129-5p and has-mir-29a-5p downregulate in contrast with their lncRNAs, but has-mir-29a-3p upregulates although its' lncRNA downregulates.

Conclusion: In other researches, COL1A1 is counted oncogene which its upregulation causes metastasis and withstand to anticancer therapy in HCC. We suggest that all miRs except has-mir-29a-3p are tumor suppressors versus their

lncRNAs that are likely oncolnc. To pinpoint that NONHSAT017523.2 was common between two miRs, causing it to be a potential biomarker for both miR detection and HCC.

Keywords: Hepatocellular carcinoma, microRNA, lncRNA, bioinformatics, COL1A1

a brief review on traumatic spinal cord injury (Review)

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Introduction: Spinal cord injury is a devastating neurological disorder with disastrous consequences for physical, social and vocational well-being of patients. over the past decades an enormous advancement has been made in our understandings of its pathophysiology and secondary mechanism. the insight given by the past researches resulted in better quality of life in patients suffering from SCI however there is still no effective therapy available and current treatment options includes the use of high dose methylprednisolone ,surgical interventions to stabilize and decompress the spinal cord rehabilitative care

Methods: in this review we outline recent advances in our understanding of the pathophysiology of SCI and some of the important consequences in addition to highlighting modern imaging tools which assist us in better evaluation of location and extent of damage. finally, we focus on novel combinatory therapeutic approaches and we discuss the efficacy of cell therapy, pharmacological interventions and tissue engineering as the main three novel procedures in SCI treatment

Results: The result of this review exemplified the feasibility of three novel approaches.. In cell therapy condition media derived from cells are considered as an alternative to cell therapy due to their more viability and less immune response stimulation compared to stem cells.in terms of anti-inflammatory drug therapy in SCI enhancement it is important to focus not only on histological healing but also on the potential of these drugs in sensory and motor function improvement.Finally regarding Tissue engineering as a good co-candidate in combined therapy in SCI there is still an urgent need for a suitable biomaterial with specific properties to be introduced in this area.

Conclusion: Traumatic spinal cord injury represents a complex pathophysiology which is in association with substantial cost and reduction in life quality. Fortunately, the care for patients have improved recently (surgical method and supportive treatment) resulting in restored function and lower pain however newer concepts claims that combinatory therapies will show better outcome compared to individual therapies therefore it is expected that through these progress SCI will be eventually repairable.

Keywords: traumatic spinal cord injury, pathophysiology, novel therapeutic approaches

A Case of Systemic Lupus Erythematosus Manifestation Following COVID-19 (Research Paper)

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Introduction: Systemic lupus erythematosus (SLE) is a complex and challenging autoimmune disease. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel viral agent that can cause a life-treating respiratory disorder named coronavirus disease 2019 (COVID-19). Association between SARS-CoV-2 and SLE is not clear. We reported the first case of SLE manifestation following COVID-19.

Methods: A 39-year-old man with complaints of fever, scaling on the palms of the hands and feet, lower extremity edema, and ankle swelling was referred to Kashan Rheumatology Clinic in 2020. Primer Laboratory tests, reverse-transcription polymerase chain reaction test (RT-PCR). Computed tomography (CT) of the chest we performed.

Results: He was infected with SARS-CoV-2 two months ago. The patients had proteinuria and was positive for SLE laboratory tests. After one week of treatment with prednisolone (30mg daily) and hydroxychloroquine, paresthesia, proteinuria, and edema continued. The patient was treated with pulse methylprednisolone (1000 mg for three consecutive days), gabapentin and vitamin B (300mg daily), which reduced paresthesia.

Conclusion: This is the first case of SLE manifestation following COVID-19. SARS-CoV-2 may produce autoantibodies or develops the clinical features of subclinical SLE.

Keywords: Autoantibodies, Autoimmune Diseases, COVID-19, Systemic Lupus Erythematosus

A comparison between Cyber knife and Rapid Arc in prostate cancer radiotherapy (Review)

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Introduction: Prostate cancer (PCa) is the second most common cancer among men all over the world. North America has the highest occurrence rate of PCa. However, Iran has the less occurrence of PCa includes 7-9% of all cancers. Various techniques of radiotherapy (RT) are established for PCa treatment such as intensity modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT). The aim of this review was to present a comparison between two novel treatment techniques: Cyber knife and Rapid Arc in prostate cancer radiotherapy.

Methods: The present review article was performed by searching “Pubmed” and “google scholar” by different combinations of terms “radiotherapy” and “prostate cancer” and “VMAT” and “cyberknife” and “rapidarc”. 40 articles were obtained. After removing the reiterative and reviewing abstracts, 22 articles were selected and reviewed full text.

Results: IMRT is the standard and most frequently used radiation modality in PCa which delivers photons in various dose distribution while reducing the surrounding normal tissue toxicity compared with conventional radiotherapy. Volumetric modulated arc therapy (VMAT) is a developmental type of IMRT with 360 degrees gantry rotation around the patient, provides high conformal dose distribution, also minimize radiation dose to organs at risk (OARs) around the tumor. A new common form of VMAT is called Rapid Arc (RA) developed to achieve precisely more radiation dose to cancerous cell during sparing healthy tissues with different dose rate and speed variations of the gantry revolution. It can be considered ideal for PCa radiotherapy. Advantages of utilizing Rapid Arc modality are high target volume coverage; faster delivery and minimum treatment time as the name reveals (lasts less than 2 minutes, approximately 2-8 times more rapid than prior techniques) due to the continuous gantry rotation, so prevent cancerous cell DNA repair; meliorating target volume conformity exclusively in targets with intricate shapes; more accurate target delivery due to time shortening which results in decreasing patient movement and target position (e.g. 4-11 minutes delivery time in lung cancer RT), improves patient comfort. But even with low dose radiation there is still the detrimental radiobiological risks; the therapeutic radiation techniques are costly as well. The clinical usage of Rapid Arc is constantly expanding. Cyberknife (CK) is a novel radiosurgery robotic device used to deliver high dose hypo-fractionated SBRT. Its first usage for PCa was done in 2003. It has been utilized to treat tumors of the pancreas, lung, spine, kidney, liver, prostate, head and neck. Although, cyber knife couldn`t be successful in metastatic recurrent PCa treatment, the benefits of this modality are high precision; late toxicity (Rare rectal toxicity and

bleeding). However, testicular toxicity may be still exists in cyber knife, but this method has better accuracy (less than 5 mm) than other external radiotherapy modalities; Patient positioning and tumor adjustment without stopping treatment during delivery due to motion robotic system is another benefit of this method. It might be expensive though.

Conclusion: Studies reveal that compared to cyber knife, Rapid Arc modality is more available and attain improved critical tissue sparing, better target dose distribution, highest dose conformity, and lower dose areas of bladder and rectum. More Scattered radiation and longest treatment and beam-on time with cyber knife (34 minutes) compared to the shortest with Rapid Arc (5.1 minutes) are obtained. Also, higher mean dose to prostate and planning target volume in cyber knife treatment method is seen. In conclusion, to decrease treatment and delivery time, RA achieves better outcomes although there`s still no apparent dosimetric priority between RA and CK, so more experimental studies are needed.

Keywords: Radiotherapy, Rapid Arc, Cyber knife, Prostate cancer

A comparison betweenTaraxacum pregrinium anticancer activity and Cisplatin against human MCF7 and Hek293 cancer cell lines (Research Paper)

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Introduction: Cancer is a chronic and non-communicable disease with genetic and acquired background. Breast cancer is the most common cancer in women and the leading cause of death. The dandelion plant with the scientific name of Taraxacum pregrinium is one of the plants that has a wide growth all over the world and its anti-inflammatory, anti-tumor, apoptotic, antioxidant and immune system stimulation effects have been proven in various researches. In Iran, Taraxacum Peregrinum species of this plant is found in abundance. Therefore, it is important to study the pharmacological effects of dandelion for further research and development on a variety of diseases, including cancer.

Methods: In this study, ethanolic extract of Taraxacum pregrinum root using 96% ethanol solvent was obtained by soaking method with a ratio of 1 to 20. Then 6 dilutions (0.01, 0.1, 1, 10, 100, 1000 and µM) of ethanolic extract of dandelion root and also 6 dilutions (0.01 to 1000 µM) of cisplatin (as one of the drugs of choice for breast cancer treatment) were prepared. The cytotoxic effects of Taraxacum pregrinum ethanolic extract and cisplatin anticancer drug were evaluated using MTT assay on MCF-7 cancer cell line (human breast cancer) and Hek293 healthy cell line (human embryo kidney). Finally, light absorption at 570 nm was read by ELISA reader and data analysis was performed by Exell software and GraphPad Prism 6.

Results: Ethanolic extract of taraxacum pregrinum root ethanolic extract was obtained during 72 hours of exposure but was not significantly effective compared to cisplatin used as a breast cancer drug in this study. But human Hek293 was not toxic to the healthy cell line either.

Conclusion: According to the results of this study, the active ingredients of the taraxacum pregrunium exhibit cytotoxic effects in different human cancer cell lines so it can be applied as Assistance treatment agent in Mcf7 cancer treatment filed.It may be possible to obtain better cytotoxic effects from this plant by changing the extraction method and solvent, the type of cancer cell line, and changing the concentration of the extract.

Keywords: MTT assay-Taraxacum pregrenium-cisplatin-Hek293-MCF7

A detailed cutaneous manifestations evaluation in polycystic ovary syndrome patients (Research Paper)

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Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. The hypothalamus-pituitary-ovary axis dysregulates in PCOS, ultimately leading to hyperandrogenisms. Consequently, it is associated with hirsutism, dyslipidemia, obesity, infertility, menstrual disturbance, and insulin resistance. To our knowledge, there is no detailed investigation on these manifestations. That is why, this study aimed to evaluate manifestations of hyperandrogenism, hirsutism in particular.

Methods: This study was performed on 39 women with an initial diagnosis of polycystic ovary syndrome. Rotterdam criteria including Oligo- or anovulation, hyperandrogenism clinical and/or biochemical signs, and ultrasound appearance of polycystic ovaries used as diagnostic criteria. Hirsutism scoring was carried out according to the Freeman-Galway's definition of the hirsutism. The patients were analyzed for other skin problems including male pattern baldness, acanthosis nigricans and acne as well as demographic features.

Results: Hirsutism was observed in the majority of our patients (91%) ranging from mild to severe. Concerning the distribution of hirsutism on various parts of the body, severe hirsutism was observed more on the groin, abdominal area, and chin respectively. Male pattern baldness, acanthosis nigricans, and acne and dysregulated menstruation were reported in these patients.

Conclusion: This investigation found that skin manifestations, especially hirsutism, are highly frequent in PCOS patients.

Keywords: polycystic ovary syndrome, hyperandrogenism, testosterone, androgen, hirsutism

A new approach for diagnosis of cystic echinococcosis based on recombinant antigens B8/1 and B8/2 (Research Paper)

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Introduction: Cystic echinococcosis (CE) is a widespread parasitic disease caused by the larval stage of Echinococcus granulosus. Since current methods for the diagnosis of CE are not efficient enough, rapid, and reliable tests are required for the acceleration of CE diagnosis. The present study aimed to produce recombinant B8/1 and B8/2 antigens of E. granulosus and evaluate their sensitivities and specificities separately and simultaneously for the diagnosis of CE.

Methods: The recombinant B8/1 and B8/2 antigens were produced and used in an ELISA system for the diagnosis of CE. The sera specimens including 30 sera from pathologically confirmed CE patients, 30 from other non-CE patients, and 30 from healthy controls, were evaluated by the ELISA, using AgB8/1 and AgB8/2.

Results: The results showed a sensitivity of 93.33%, 90%, and 96.7% for AgB8/1, AgB8/2, and their combination, respectively. The specificities were 91.7%, 93.33%, and 93.33% for AgB8/1, AgB8/2, and their combination, respectively.

Conclusion: Simultaneous usage of AgB8/1 and AgB8/2 increased the test sensitivity for the diagnosis of CE. Furthermore, the specificity of AgB8/1 and AgB8/2 combination was more than AgB8/1 and equal to AgB8/2 alone. The findings revealed that the simultaneous usage of AgB8/1 and AgB8/2 could be a suitable approach for the diagnosis of CE.

Keywords: Diagnosis; Cystic echinococcosis; Recombinant antigen B

A new approach to cancer therapy with lipo-cell (Research Paper)

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Introduction: Cisplatin is one of the essential drugs for the treatment of solid tumours. In humans and animals, it causes damage to the kidneys, bone marrow, hearing, respiratory system, and DNA of cells, which is one of the causes of infertility. In this study, we used modern medical methods to synthesize artificial cells of the liposome type. Artificial lipo cells were not detected by the immune system and were able to remove tumour cells successfully. It also significantly reduced the side effects of the drug.

Methods: We optimized five formulas for liposomes by modifying the ratio of SPC80 (soy phospholipids to 75% phosphatidylcholine) and cholesterol. Then the best liposomal formulations of PEGylated novels containing SPC80: Cholesterol: DSPE-MPEG (in a ratio of 85: 10: 5) are designed and manufactured to improve as a treatment to achieve better drug efficacy.

Results: Zeta Sizer showed that PEGylated nanoliposomes had a mean diameter of five formulas approximately 100 nm, a zeta potential of -26.03 ± 1.34 mV, and entrapment efficiency of 96.65 ± 3 %. The optimum formulations represented sustained, thermosensitive release, and augmented cellular uptake. The cytotoxic effect of the liposomal drug was higher than that of the free medication drug, which confirmed the efficiency of cellular uptake.

Conclusion: This study suggests that drug carriers such as synthesized nano-liposomes play an essential role in drug efficacy and dosage reduction.

Keywords: lipo-cell, Nano-liposome, Cancer, Cisplatin

A regulation of Nodal/ Activins in the tumorigenesis process by Piwil2 (Review)

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Introduction: Epithelial-to-mesenchymal transition (EMT) has been reported to a vital program in both embryonic development and cancer progression. Recently, a wide range of studies has highlighted a link between EMT and the formation of cancer stem cells (CSCs), a small subset of tumor cells with SC-like properties. Various Signaling pathways are connecting EMT programs to stemness properties. One of which is TGFβ superfamily members, such as NODAL and Activin. Nodal/ Activins are expressed during embryonic development, but their aberrant re-expression induce the CSCs formation and EMT process. Another fundamental inducer of CSCs and Epithelial-to-mesenchymal transition is PIWIL2, a member of the piwi gene family. PIWIL2 is normally expressed in the testis and regulated self-renewal in germ cells, but its ectopic expression has been reported in a variety of tumors where it affects the initiation and progression of cancer. Although, Based on previous studies, PIWIL2 negatively regulates TGF-beta signaling, including NODAL in early embryogenesis, the role and the relationship between piwil2 and TGF-beta family are not understood in the process of tumorigenesis.

Methods: Therefore, Our objective is to review the recent articles for discovering the upstream regulatory function(s) of Piwil2 in TGFβ members expression in carcinogenesis.

Results: The findings presented here suggest that the regulatory functions of piwil2 in the Nodal/Activin signaling pathway.

Conclusion: The findings presented here suggest that the regulatory functions of piwil2 in the Nodal/Activin signaling pathway. However, further experimental data are needed to fully confirm the regulatory role of piwil2 in the pathways.

Keywords: piwil2, EMT, CSC, Nodal, Activin.

A review of Breast cancer in men and the most important microRNAs involved in this cancer (Review)

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Introduction: Breast cancer is a very rare disease in men. This is probably due to the smaller amount of breast tissue and the fact that men produce lower amounts of hormones such as estrogen, which have been shown to affect breast cancer in women. However, only one in 100 cases of breast cancer occurs in men, and out of one million men, only 10 people get the disease. Breast cancer is very rare for men under the age of 35, but the risk increases with age. In fact, men get the same type of breast cancer as women and which involves different profile changes in both mRNA and micro-RNA (miRNA) expression. Non-coding RNA based regulation is a newly discovered way of genome regulation which includes microRNAs, lncRNAs, siRNAs, and piRNAs. MicroRNAs or miRNAs are 21-23 nucleotide non-coding RNAs with clear function in cell division, differentiation, and apoptosis. The RNAs are responsible for post-transcriptional regulation, typically through sequence-specific interactions with 3' untranslated region of mRNAs. In this study, breast cancer in men and the most important microRNAs involved in this cancer will be investigated.

Methods: In this study, the method of library collection, search in various texts and authoritative scientific articles has been used.

Results: Male Breast cancer (MBC) is a rare disease in men, representing less than 1% of all malignancies and responsible for 0.1% of male cancer deaths and it has a more aggressive clinical behavior compared with female breast cancer. MicroRNAs (miRNAs) are a class of small noncoding RNAs that control gene expression by targeting mRNAs and triggering either translation repression or RNA degradation. There have been many studies on the expression of various miRNAs and their roles in breast cancer. Previous studies have demonstrated that there is a large number of deregulated miRNAs in human breast cancer (in particular, miR-10b, miR-17-5p, miR-21, miR-27a, miR-27b, miR-125a, miR-336, miR-10b, miR-126, miR-125a-5p, miR-125b and the let-7 family). Studies show that miR-499-3P and miR-330-5p are among the major microRNAs in male breast cancer. Other important microRNAs that may be involved in this cancer include miR-191, miR-10b, miR-218, miR-140-3p and miR-126. Only few studies have been reported regarding miRNA expression profiling in MBC. From a histological point of view, male breast cancer is usually an invasive ductal carcinoma. This histotype specificity seems one of the major differences between male and female breast cancer biology. In this regard, some studies analyzed the miRNA expression profiles of male/female breast cancer samples, looking for miRNAs differentially expressed between the two clinical categories. Previous studies of miRNA expression in human breast cancer have focused on comparing normal tissues with

tumor samples Studies show that some microRNAs, such as miR-10b, can increase the incidence of breast cancer in women by inducing tumor invasion and metastasis of breast cancer-derived cells, and this can also affect breast cancer in men. Studies show that a number of microRNAs in breast cancer are upregulated, such as miR-149 and miR-29b, and others are downregulated, such as miR-145, miR-10b, let-7g, which are being studied in laboratory studies. In the last part of this section, we will explain the most normal way to control breast cancer in men. Gynecomastia means excessive breast enlargement in men. This type of breast enlargement is mostly due to the growth of mammary glandular tissue, not much adipose tissue due to obesity. Gynecomastia could be considered a good normal control for male breast cancer. Numerous conditions have been associated with gynecomastia, but the pathophysiological bases are due to an imbalance of sex hormones and the tissue responsiveness to them.

Conclusion: MiRNAs, as mRNA regulators, could serve as novel diagnostic and prognostic candidates, and potential therapeutic targets in breath cancer. In this study, we tried to give a brief and useful study of breast cancer in men and the microRNAs involved in this cancer.

Keywords: MBC, miRNAs, Gynecomastia

A review of menstrual health and its promotion in adolescent girls (Review)

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Introduction: One of the most important periods of life is adolescence and puberty. Adolescence as the second decade of life is associated with severe physical, sexual and psychosocial changes. Menstrual health and self care are important aspects of adolescent health that determine health status and adherence to hygiene practices in adulthood. The aim of this study was to identify menstrual health ways to improve it.

Methods: This study is a review study that was conducted in 1399. The data of this study using the keywords, Menstrual health, Health promotion, juvenile at Google scholar, SID, Magiran databases were collected and analyzed

Results: Lack of knowledge of adolescent girls about the mechanisms of puberty and menstruation causes physical, psychological and behavioral problems in them. Lack of menstrual hygiene and improper self-care practices are complications of this age group and factors such as lack of proper knowledge about menstrual health lead to incorrect functions during this period. Awareness of menstrual health is influenced by various factors such as cultural and religious beliefs, parents education level, parents' job, place of residence, etc. Also awareness of the characteristics of this period directly affects the type of health performance of girls. Studies show that adolescent girls gain more information about menstruation and health performance during this period than their parents, especially mothers, and to a lesser extent from the content of magazines and books, But in some cases, cultural and religious beliefs prevent the exchange of information about menstruation and menstrual health between adolescents and parents.

Conclusion: Observing proper menstrual hygiene requires knowledge about its principles and According to sources such as parents and school educators from whom adolescent girls obtain major menstrual information; Educate them about menstrual hygiene and refer to it as a natural event away from incorrect cultural and religious beliefs and also direct education is offered to adolescents through appropriate educational methods such as media, social networks and publications.

Keywords: Menstrual health, Health promotion, Adolescent.

A review of Nucleic acid aptamers in diagnosis of colorectal cancer (Review)

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Introduction: Aptamers are relatively small biomolecules (oligonucleotides ranging from 20 to 170 nucleotides or peptides with 12 to 30 amino acid residues) or short sequences of nucleic acid which have a unique three-dimensional structure that is influenced by their sequence and this structure affects the binding of aptamers to theirs specific ligands with High tendency and high specificity. Small size and fast and cheap production process along with high stability, ease of chemical production, simple storage and resistance to denaturation have made them attractive molecules in cancer research fields. Aptamers isolated from large combinatorial libraries through the Systematic Evolution of Ligands by Exponential enrichment (SELEX) procedure. Colorectal cancer (CRC) is one of the most common cancers worldwide with an estimated 1 million people diagnosed annually. In the world, colorectal cancer accounts for 9.5% of cancer rates in men and 10% of this rate in women and this cancer is considered as one of the most important cancers in both sexes. Although the effectiveness of current treatments for colorectal cancer is very low, early detection can help prevent it from growing rapidly in the body. This study Review recent advances in the development of nucleic acid aptamer-based methods for diagnosis and prognosis of colorectal cancer.

Methods: In this study, the method of library collection, search in various texts and authoritative scientific articles has been used.

Results: Nucleic acid aptamers are a class of high-affinity nucleic acid ligands and they can be used in laboratory research and in clinical diagnosis and treatment. Colorectal cancer (CRC) is the most frequently diagnosed cancer which causes many deaths in the world every year. Circulating carcinoembryonic antigen (CEA) is a tumor-associated glycoprotein antigen that has been used in clinical diagnosis and prognosis of CRC and it is first blood biomarker used for CRC detection. There are many studies which have developed aptamer-based diagnostic systems for detection of CEA. Circulating tumor cells (CTCs) are considered to play a key role in metastasis of cancers such as colorectal cancer and some aptamers like SYL3C can play role in isolation of them. MUC1 aptamer is a DNA aptamer specific for mucin-1 and is used for colorectal cancer DLD-1 cells. The PDGF aptamer has high promise to be used as an effective and specific inhibitor of PDGF in cancer therapy. Overexpression of PDGF-BB is associated with the development of colorectal cancer. Fluorescently labeled KCHA10 and KDED2a-3 DNA aptamers that they can also be used to diagnose some colorectal cancer cells. 488-labeled YJ-1 is one of the aptamers for capturing colorectal cancer cells. Fluorescently labeled anti-EpCAM DNA aptamer (SYL3C-CY3) as an effective probe for diagnosis of EpCAM-positive CRC cells in tissue samples derived from patients with CRC. A DNA aptamer named J3 labeled with Cy5 fluorescent dye is an excellent probe for

imaging of tissue sections derived from CRC patients. XL-33-1 is also one of the aptamers that has a similar approximation capability to J3 aptemer. Fluorine-18 is one of the aptamers that binds to the extracellular domain of protein tyrosine kinase 7 (PTK7) and PTK7 is a transmembrane protein overexpressed in CRC. 5TR1 aptamer is one of the aptamers for in vivo MR imaging-guided drug delivery in a murine colorectal carcinoma model. There are many other aptamers that can be used to diagnose and treat cancers, especially colorectal cancer and further studies on them can further enhance their value.

Conclusion: Aptamer technology is a tool with new and extraordinary capabilities that help them in the diagnosis and treatment of various diseases, including cancers such as colorectal cancer. This review covers the reported applications of nucleic acid aptamers in the diagnosis of colorectal cancer. Given that many studies have been conducted on the importance of aptamers in the treatment of cancers, especially colorectal cancer, and this shows the importance of their existence. Further researches could shed more light on the importance and benefits of using aptamers in the treatment and diagnosis and prevention of colorectal cancer.

Keywords: CRC, Aptamer technology, Diagnosis

A review of prevalent drug–drug interactions in elderly patients with hypertension (Review)

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Introduction: Elderly people are in risk of drug-drug interactions because of age-related physiological changes, incidence of high chronic diseases prevalence such as hypertension and polypharmacy. drug interaction in elderly patients is a concerning problem that would be reduced by carefully monitoring the patient and adverse drug effects. The aim of this review is to study the potential drug interactions in elderly patients with hypertension.

Methods: 43 articles about hypertension and drug interactions in elderly people from PubMed and Google Scholar was reviewed.

Results: Hypertension is one of the most prevalent diseases among the elderly people . Drugs such as angiotensin converting enzyme inhibitors(ACEIs) , angiotensin-receptor blockers (ARBs), calcium channel blockers (CCBs), beta-blockers, and diuretics are the most frequent anti-hypertensive drugs. There is the risk of potentiating hypotension with the additive use of two or more antihypertensive medications. The antihypertensive effect of blood pressure medications can be increased or decreased by using different type of agents. The most relevant interactions involving common antihypertensive medications includes: non steroidal anti inflammatory drugs , Anti hyperglycemics, antibiotics , Loop diuretics ,potassium sparing diuretics, Cyclosporine , Carbamazepine, Digoxin, Theophylline, warfarin, and Lithium. Severity of drug interactions between men and women is different because of pharmacological differences.

Conclusion: Drug interactions and adverse drug effects associated with hypertension is one of the most frequent problems among the elderly patients all over the world.Caution must be taken when initiating and prescribing medications for Hypertension in the elderly.

Keywords: Elderly, Hypertension, Drug interactions, Pharmacodynamic, Adverse drug effect

A review of the clinical applications of gamma polyglutamic acid (Review)

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1.

Introduction: Polyglutamic acid (PGA) is a natural biopolymer composed of duplicate units of L-glutamic acid, D-glutamic acid, or both. Different types of bacteria produce this polymer, each of which has a unique property. It has two isoforms of gamma polyglutamic acid (γ-PGA) and alpha polyglutamic acid (α-PGA) . γ-PGA exhibits different properties (conformational modes, antimicrobial properties, and molecular weight). Due to the specific nature for example biodegradable , non-toxicity is used in the food, medical and water industries. In clinical applications, α-PGA has been used for drug delivery. γ-PGA is essentially different from α-PGA and is resistant to proteases. Other applications include the role of gene transfer. The various applications of this polymer depend on its structure and shape. In this study, the factors affecting the structure and clinical applications of gamma glutamate have been investigated.

Methods: In this study, studies related to gamma polyglutamic acid from pubmed databases over the past few years were reviewed. Factors affecting the structure that cause variation in the application of this biodegradable polymer and its clinical applications were investigated.

Results: This polymer is produced by different species of bacteria and in each species has a unique molecular weight and structure. This structural diversity has led to diversity in its application. Due to its properties, this polymer can be used in various industries such as food, pharmaceutical and medical industries. Factors affecting its structure include ionic strength, concentration and pH. In fact, PGA has a very sensitive structure. Hydrophilicity and high reactivity play an important role in biological functions and unusual structural properties.

Conclusion: Gamma polyglutamic acid nanoparticles are used as carriers of anti-cancer drugs. Nanoparticles made from gammaglutamic acid have received a great deal of attention due to their ease of production and purification and their suitable biological properties. In new gene transfer systems, cationic complexes coated with polyglutamic acid nanoparticles are used for more effective and safer treatment. Design of microneedle structures based on gamma-glutamic acid can be a tool to improve subcutaneous insulin injection. The results of studies show that γ-PGA increases calcium solubility and thus increases calcium absorption in mice.

Keywords: : glutamic acid, γ-PGA, α-PGA, biodegradable, drug delivery.

A review of the type and degree of Hearing loss in patient with Alport syndrome. (Review)

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Introduction: Alport syndrome (AS) includes a group of hereditary diseases caused by mutations in the COL4A3, COL4A4 or COL4A5 genes. These genes are responsible for the biosynthesis of α3, α4 and α5 collagen IV chains, which are located in the glomerular basement membrane of the kidney, the inner ear and the eye. Alport syndrome is caused by mutations (changes) to specific genes before a child is born. In this article we synthesise the main features of deafness associated with Alport syndrome.

Methods: This study is a review of the Hearing loss caused by Alport syndrome, by analyzing articles from dependable scientific databases,includingGoogleScholar, ScienceDirect,PubMed, and Scopus.

Results: Hearing loss is one of the first signs of AS. It becomes evident at the end of childhood or beginning of adolescence in boys with X-linked disease and the progression suggests poor prognosis of renal disease.Hearing loss caused by alport syndrom is sensori neural ,bilatral,symetrical and progressive. It was observed in 55% of men and45% of women.configuration of the Hearing loss in Alport syndrome in audiometric studies.

Conclusion: The concept of hearing loss severity must be redefined, as there is a clear need for more active hearing management in Alport's syndrome patients with severe and profound hearing loss. Sensorineural hearing loss (SNHL) caused by Alport's syndrome generally does not exceed 60-70 dB, because a cochlear lesion is responsible for this hearing loss. Careful management of renal function improves the prognosis and the longevity of Alport's syndrome patients; it is useful to reassess SNHL caused by Alport's syndrome. The level of hearing is positively correlated with disease duration. The otologist should follow up these patients. Ophthalmologic and genetic examinations should be ordered to provide counseling to the patients and the family members.

Keywords: alport syndrome,hearingloss,mutation,sensorineural hearing loss.

A review on Coronavirus (Review)

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Introduction: Today, the novel coronavirus (COVID-19) has caused a pandemic with significant morbidity and mortality. Coronaviruses are large, coated viruses that contain RNA. Human coronaviruses cause the common cold. They may cause lower respiratory tract infections and are involved in pediatric gastroenteritis. New coronaviruses have been identified as the cause of Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). In domestic animals, animal coronaviruses can cause economically significant diseases, and in lower animals, they could cause persistent infections. Coronaviruses are difficult to culture and therefore their characteristics are not well understood. In 2003, the outbreak of the SARS became a severe respiratory illness with progressive pneumonia and respiratory failure. The virus was also found in other organs such as the kidneys, liver, small intestine, and feces. The SARS virus probably originated from non-human sources such as bats, which multiplied and transmitted to humans in wet shops. In rural areas of southern China, where the pandemic began, humans, pigs, and domestic chickens are living side by side, people hunting wild species for food and traditional medicine and this might cause the new viral strain. COVID-19, also known as Acute Respiratory Disease Cone-2019, is an infectious disease caused by acute coronavirus syndrome (SARS-COV-2). Common symptoms are fever, cough, shortness of breath, and, more recently, numbness. Mortality rates are estimated at between 1% and 5% but vary with age and other health conditions. Animals sold for food are thought to be the source or mediator of the virus because many of the people who were infected at first were workers in the Hovanna seafood market.

Methods: Using keywords: virus, coronavirus, COVID-19, etc. Browsing related articles, journals, and books to gather information about astroviruses, including the extent of the damage, the prevalence of the disease.

Results: In adults, human coronaviruses usually cause a fever-free cold. The incubation period of this disease is about 2-5 days and the symptoms usually last about a week. SARS-CoV causes severe respiratory illness. The incubation period of the disease is 6 days. Common early symptoms include fever, restlessness, chills, headache, dizziness, cough, and sore throat, followed by shortness of breath a few days later. MERS-COV causes mild to severe respiratory disease in children and adults. Patients with more severe illnesses are affected, as is the case in the elderly. The incubation period is 12-13 days, in some cases, the disease is long and leads to pneumonia and death.

Conclusion: There is no approved treatment or vaccine for the COVID-19 infection. Protease inhibitors are effective in treating human immunodeficiency virus infections (such as Lopinavir) in vitro against the SARS. The SARS vaccines have being to develop. Effective control measures to curb the spread of SARS include: isolating patients, quarantining people who have been in contact with infected people, restricting travel, and the use of gloves, goggles, and respirators by health care workers.

Keywords: Virus, Coronavirus, COVID-19.

A review on proton therapy advantages in treatment of pediatric cancer (Review)

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Introduction: Cancer is the second cause of death in children under the age of 15. The majority of pediatric oncology concepts includes curative aims and long-term survival besides minimizing treatment-related side effects to improve quality of life. Radiotherapy (RT) is important in children because immature childhood tissues exacerbate destructive radiation effects on growth, intelligence quality and endocrine system. Particle therapy due to its exclusive physical features is recommended for pediatric radiation therapy which involves carbon ion therapy (CIRT) and proton therapy (PT). Therefore, the aim of this review was to evaluate the proton therapy in treatment of pediatric cancer.

Methods: The present review article was performed by searching “Pubmed” and “google scholar” by different combinations of terms “particle therapy” and “pediatric cancer” and “proton therapy” and “carbon ion therapy”. 28 articles were obtained. After removing the reiterative and reviewing abstracts, 12 articles were selected and reviewed full text.

Results: Particle therapy is less dependent on presence of oxygen in cancerous cell, thus could be effective on hypoxic tumors. Due to high local dose in the target place (Bragg-peak), minimal low integral dose in other depths, particle therapy is significantly superior to conventional radiotherapy with photons, so results in sparing uninvolved tissues, decreasing acute and late radiation related sequels and eventually reducing the incidence of secondary malignancy which is one of the critical concerns of pediatrics radiation therapy; As studies had shown that radiotherapy increases probability of incidence of secondary sarcoma in children with hereditary retinoblastoma. Proton therapy has been done in various modes such as pencil beam, scattering and uniform beam, on children with tumors of CNS(ependymoma, neuroblastoma, germ cell tumors, medulloblastoma), eye, soft tissue and bone sarcomas of head and neck and paraspinal or pelvic regions. PT provides higher tumor dose distribution, lower toxicities and shorter treatment times (hypo-fractionation). Meanwhile, in PT the expected sever toxicities from other RT modalities are rare; fewer mild side effects are related to the size and location of the lesion and almost disappear during the first six months or remain at a very low level. Grade IV acute toxicity reaction (bone marrow) might be revealed in patients received chemotherapy concurrently. Leading patient’s complications probably are hair loss in patients with superficial lesions, dermatitis, dizziness, headache, mucositis and hearing loss. Except in specific cases, e.g. osteosarcoma, the main pediatric treatments are with protons. Substantial to know that in whole-brain RT for metastatic cancers or for acute leukemia, PT has no more priority than photons.

Also, the procedure is accomplished under general anesthesia (for all children preferably) due to children difficulties to remain immobile.

Conclusion: Although, PT could be expensive, however; it may lead to economic benefits by less irradiation, salvage surgery and palliative chemotherapy. Particle therapy is a considerable method used for radio-resistant and deep located tumors and the ones with adjacency to sensitive organs such as osteosarcoma due to its greater biological effectiveness. To assess the long-term potential of particle therapy in pediatric patients needs much longer pursue in the future.

Keywords: Particle therapy, Proton therapy, Pediatric cancer

A Review on the Effects of Somatic Stem Cells, Herbal Medicines, and Genes on Human's Age Increase (Review)

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Introduction: Aging is a general irreversible phenomenon, which is accompanied with some of the aging-related diseases such as Alzheimer, cardiovascular problems, blood pressure and etc. Various peripheral and internal factors of the body are influential in the human's aging process. Senescent through tissue-specific stem cell sections is reliable to play a main role in the pathophysiology of Senescent in many tissues via a decreasing inclusion to intercede normal homeostatic tissue maintenance and regenerative response. Additionally, eukaryotic cells chromosomes' end wearing (Telomere) play a key role in aging process. Moreover, herbal medicines have important anti-aging function. Furthermore, researchers have identified the role of various genes in aging process. Increased lifespan and immortality is a perpetual puzzle and various studies have been conducted over the time in line with human's life increase, since identification of the mechanism and its influencing way of aging process might provide the conditions for invention of a method in order to increase human lifespan. According to the finding of the past studies, it was revealed that the main factors in increased human lifespan are having a healthy life plan such as avoiding free radical factors' generation in the body, using foodstuffs rich with antioxidants, avoiding stress and having gene resistant to mutations.

Methods: In this review we used online database such as NCBI (PubMed), and Google scholar. This Research is the result of a survey of more than 125 articles of which 84 articles are directly used in this study.

Results: Avoiding stress, free radicals and environmental mutagenic factors, and also using foodstuffs rich with antioxidants are the most important secrets of increased lifespan. Moreover, safekeeping from chronic illness of senescent includes antioxidant functions, mitochondrial stabilizing activates, metal chelating functions, suppression of apoptosis of biotic cells (important type of aging-related stem cell), and instigation of cancer cell apoptosis. Furthermore, wide genetic, chemical, physiological and etc. studies conducted in the field of increased lifespan of human can increase life expectancy and lifespan, preventing aging-related diseases.

Conclusion: In this article, human lifespan increase process, different peripheral and internal factors in the body, which cause decreased lifespan of human was investigated. Consequently, we will have healthy old age life, which lacks aging-associated disease by relying on the conducted studies and researches.

Keywords: Aging, Somatic stem cells, Free radical, Antioxidant, Telomere

A Sensitive and Selective Electrochemical Biosensor for Detection of MicroRNA-181a as a Very Critical Biomarker for Detection of Some Cancers (Research Paper)

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Introduction: MicroRNAs (miRNA) are short, noncoding, single strand RNAs and they have very vital roles in proliferation, apoptosis, differentiation and gene silencing. This kind of RNAs can use as cancer biomarker. mir181a, a kind of miRNA, is a biomarker to detection of some cancers such as gastric cancer, colorectal cancer, breast cancer metastasis, epithelial ovarian cancer (EOC), hepatocellular carcinoma (HCC) and acute myeloid leukemia (AML). Dysregulation of mir181a is an important marker for mentioned cancers. Therefore, analyzing of this biomarker is very useful for clinicians, because they can detect some cancers (as mentioned above) in the early stage.

Methods: Biosensors are very useful and very sensitive devices and researches use it medicine for detection of diseases, for example cancer. Detection of cancer in the early stage is vital because curing of cancer in early stage is simple. In this regard, we developed an electrochemical DNA based biosensor for detection and capturing of miRNA181a. For this aim, we used polypyrrole (PPy) and antimiRNA-181a probes (were used as target (miRNA-181a) capturing element) on glassy carbon electrode (GCE) and methylene blue (MB) as electroactive label in electrochemical analyze.

Results: In this research, electrochemical techniques (CV, DPV), AFM and FTIR spectrophotometric techniques were used for modification of electrode and approving of biosensor preparation steps. After passing the optimization of all experimental parameters, the modified electrode after an overnight duration analyzed by DPV technique and stability of it confirmed. Selectivity of biosensor verified by DVP technique by using of non-complementary microRNAs (designed biosensor connected only to target microRNAs) and sensitivity (3 ppm) of the designed biosensor for target microRNA analyzed by electrochemical techniques.

Conclusion: The designed biosensor in this research is very sensitive, selective, inexpensive, repeatable and has fast response time. Therefore, this biosensor can detect very low concentration of miRNA-181a. Therefore, it is a very useful analytical device for early detection of cancers in clinical laboratories and help to clinicians to treatment of patients.

Keywords: Cancer, Electrochemical Biosensor, Biomedical Analysis, MicroRNA-181a

A simple suitable microfluidic devise for investigating the effect of shear stress on the stem cell differentiation to the chondrocyte cells (Research Paper)

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Introduction: Cartilage and joints disorders are very common among people [1]. Tissue engineering today provides a new solution for cartilage regeneration based on the use of a combination of cells, scaffolds, and biomolecules [2, 3] that needs a good number of the cellular source. The number of patient chondrocyte cells is not enough for transplant, and donors are usually scarce. On the other hand, stem cells of unlimited proliferation, simple culture, and chondrocyte differentiation can be considered as a suitable source for the production of chondrocyte cells [4]. The microfluidic devices provide the conditions of applying the chemical and mechanical stimuli to the cell differentiation[4] [5], [1] [7] . The differentiation of chondrocyte cells within the bioreactor under mechanical stimulation of compressive and shear forces has been investigated [8] and showed that shear stress alone reduces the process of the cell differentiation in that situation. However, from the mechanical point of view, the shear force is not uniform in that case, so it is not possible to properly assess the effect of the shear force on the cell differentiation. In the present work, a simple microchip is designed and fabricated to create a uniform shear force on the cells.

Methods: The mold of the microchip has been created by CNC on PMMA (Polymethyl methacrylate). The microchip has fabricated by molding method using polymeric PDMS (Polydimethylsiloxane). This microchip consists of a main channel with a rectangular cross-section. The length, width, and height of the main channel are 2 cm, 1 mm, and 500 μm, respectively. The cells will be cultured on the floor of the channel, and the culture medium passes through them to exerts shear forces on the cells. The microchip has been connected to a syringe micro-pump. The syringe micro-pump inserts the culture media into the microchannel with the controllable amount. The shear stress distribution on the cells in the microchip is modeled with the computational fluid dynamic simulation. The amount of shear stress has been controlled by the flow rate by the syringe micro-pump.

Results: It is shown that the shear stress distribution on the cells is almost uniform for a flow rate of 1 to 100 μl/min. The variation of the shear force on the cells embedded in the floor of the channel is plotted against the mass flow rate of the culture media on fig. For a flow rate of 1 to 100 μl/min the shear stress varied linearly from 0.0005436 to 0.05432 Pa. The amount of shear stress is controlled by the flow rate that can be adjusted by the syringe micro-pump.

Conclusion: The data show that the shear force on the floor of the microchannel is almost uniform. The amount of shear stress is easily controlled by the mass flow rate. This simple microchip proved the condition to investigate the effect of the pure shear stress on the differentiation of stem cells into chondrocyte cells. As the future

work, we plan to culture the stem cell on the microchip and study the effect of shear force and chemical stimulation in the cell differentiation to the chondrocyte cells.

Keywords: Microfluidic, Chondrocyte cells, Stem cell differentiation, Mechanical stimulation

A study on hyaluronic acid/hydroxyethyl cellulose tissue engineering scaffold for wound healing (Research Paper)

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Introduction: Wound healing is an active process including several phases and procedures for recovering epidermal tissue and cellular structures of injured site to its initial function and formation (Choi et al. 2008). Hydrogels are typically composed of hydrophilic polymers, such as hyaluronic acid (HA) and hydroxyethyl cellulose (HEC). Swollen hydrogels absorb large quantities of water without dissolution and they feature unique structural properties, which are similar to those of tissues and the extracellular matrix (ECM) of the skin. The unique properties of hydrogels, make them suitable for applications as biomaterials for scaffolds in the tissue engineering (Kwon et al. 2015). In modern fashion of wound management systems, one of the most important factors to achieve healing quickly is a moist environment. This condition mounting migration of epidermal cells with enhanced laid-up of necrosis tissue and fibrin, promoting angiogenesis, and collagen synthesis, provoking fibroblast mitosis (Katz et al. 1991).

Methods: Hyaluronic acid (average Mw = 1.2 MDa) was a kind gift from Chitotech (Tehran, Iran). Hydroxyethyl cellulose (average Mw = 90,000 Da) was purchased from Sigma Aldrich (USA). ɣ- glycidoxypropyltrimethoxysilane (GPTMS) was purchased from MERCK (USA). Scaffold preparation HA/HEC complex hydrogel was prepared by weight ratio of HA to HEC by 50:50 which was coded as HA50-HEC50. They were dissolved completely in 20 mL deionized water by stirring, to achieve a homogeneous solution (rpm: 250, for 6 h at room temperature). Then, the GPTMS cross-linking agent was added drop-wisely into the solution with a 10% (w/w) of polymers and further stirred (rpm: 100, for 48 h at 60˚C). Then, the obtained solution poured into a petri dish and pre-frozen at -80˚C in a deep freezer. The frozen samples were lyophilized (FD-10, Pishtaz Engineering Co. Iran) at a temperature of -58 °C and pressure 0.5 torrs for 48 hours.

Results: Scanning Electron Microscopy (SEM) Fig. 1 demonstrated the surface morphology of the scaffold, which was conducted by using SEM. The scaffold structure exhibited heterogeneous porous patterns. It depicted that pores were continuous and well interconnected and the average pore size was in the range of 50-120µm, which leads to a large swelling ratio (Kim et al. 2003). Swelling ratio (%) Properties of the swelling behavior of the scaffold were determined by (Türe 2019) as shown in Fig. 2. The swelling ratio was found to 1650% and then reached to 2500% in 6 hours. The swelling of super-porous structure is due to capillary forces,

which lead to rapid uptake of water that exists mainly as free water (Omidiana et al. 2005). Hydrophilic groups of HA (COOH, OH), HEC (OH), and GPTMS (OH) were other reasons for enhancing this ratio. GPTMS with longer molecular chains (epoxy) would provide the structure with more ability to expand and swell (Poursamar et al. 2016). The ability of the scaffold to absorb a large quantity of water helps to hydrates the wound and absorbed excess wound exudate. In vitro wound healing The results demonstrate that scaffold significantly enhanced the migration rate of L929 cells and that after 24 h the wounded area in presence of scaffold was closed by 65% compare to control and positive control (culture medium) (Fig. 3). The obtained images were quantitatively analyzed with the WimScratch online software program. The migration rate of fibroblast cells towards the wounded site is an important factor that can accelerate the healing process after injury which were happened due to moist environment.

Conclusion: In this study, we prepared a super porous tissue engineering scaffold for wound healing. It exhibited the large water uptake due to functional groups, structure, and high pour size. Moreover, the scaffold exhibited remarkable in vitro wound contraction potential in terms of improved fibroblast cell migration.

Keywords: Hyaluronic acid, Hydroxyethyl cellulose, Wound healing, Tissue engineering,

A survey of women's knowledge and attitudes about obsessive-compulsive disorders (Research Paper)

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Introduction: Obsession is an idea or a repetitive movement that is accompanied by a feeling of inevitability of the mind and a desire to resist it. Studies have shown that, Mental disorders are equal in men and women, but obsessions, especially Germaphobia, are more common in women. Many people are affected by this disorder for years without realizing it. The present study examines the level of women's awareness of obsession.

Methods: This study was descriptive accompanied by questionnaires. The sample of this study included 200 women in the 20 to 35 age group who were randomly selected. Individuals were asked to answer a questionnaire containing 4 questions about their awareness of obsessive-compulsive disorder. At the end of sampling, the results were analyzed.

Results: The results of the evaluation of questionnaires related to women's awareness of obsessive-compulsive disorder show that 67.5% of the samples do not accept obsessive-compulsive disorder as a mental disorder and consider it as a normal behavior. Also, 60.42% of people are not Aware of the dimensions of this disorder and 70.83% have suffered from obsessive thoughts of themselves or their relatives and finally 72.91% of the samples want to learn and teach the dimensions and principles of obsessive-compulsive disorder.

Conclusion: According to research, a large percentage of women do not consider obsessive-compulsive disorder as a mental disorder and are not aware of obsessive-compulsive disorder, and they have also suffered from obsessive thoughts about themselves and their families. Given that obsession is one of the disorders whose treatment is based on the acceptance of the disease, the need for awareness and acceptance by the individual and those around is quite obvious; Therefore, the isolation of the obsessive person in the community and family can be prevented by careful and purposeful planning to provide education and break the obsession taboo in society and also to state that obsession is treatable.

Keywords: Women's mental health, obsessive-compulsive disorder, women's attitudes toward obsessive-compulsive

A systematic review of the role of nutritional patterns in mental health (Review)

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Introduction: Nutritional patterns as one of the most important aspects of health have a great impact on physical and mental performance. The role of dietary patterns and consumption of different food groups on mental health in different populations is very important. Therefore, the present study was conducted with the aim of a systematic review of the role of nutritional patterns in mental health.

Methods: The present study was conducted by systematic review. Using the keywords (Health OR Mental Health) (diet OR nutrition OR food), (pattern OR habit OR behavior) in the databases Elsevier, Science Direct, Pubmed, Scopus, Googlescholar, SID and after removing duplicate and irrelevant articles, 20 full-text articles published between 2000 and 2020 were reviewed.

Results: Two types of healthy and unhealthy eating patterns were effective in mental health. Healthy eating patterns such as dairy, fruits, vegetables and meat (fish), omega 3, folate, B vitamins (B6 and B12, niacin), vitamins D, C, A, E, antioxidants, legumes, nuts , Grains and unsaturated fats such as olive oil are effective in increasing mental health. An unhealthy diet, such as consuming too much saturated fat and sugar, has a negative effect on mental health.

Conclusion: There is currently little evidence linking mental health and nutritional patterns. Therefore, it is difficult to Conclusion and definitive research in this regard. Also confounding factors such as age, sex, education level, severity of obesity, economic status, smoking, alcohol and social support are effective in predicting mental health. More detailed studies are needed to investigate the impact of these factors on mental health.

Keywords: food groups, nutrition patterns, mental health

Abrogation of histone deacetylases (HDACs) decreases survival of chronic myeloid leukemia cells (Research Paper)

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Introduction: Although the identification of tyrosine kinase inhibitors has changed the treatment paradigm of many cancer types including chronic myeloid leukemia (CML), still adjustment of neoplastic cells to cytotoxic effects of anti-cancer drugs is a serious challenge. In the area of drug resistance, epigenetic alterations are at the center of attention and the present study aimed to evaluate whether blockage of epigenetic mechanisms using a pan-histone deacetylase (HDAC) inhibitor induces cell death in CML-derived K562 cells.

Methods: in order to evaluate the effect of Panobinostat on CML cells, K562 cells treated with Panobinostat. then cell survival was evaluated using Trypan blue exclusion assay and MTT assay. The distribution of treated cells in different-phase of cell cycle was evaluated using PI standing.

Results: We found that the abrogation of HDACs using panobinostat resulted in a reduction in survival of the K562 cell line through p21-mediated G1 cell cycle arrest.

Conclusion: The results of the present study shed new light on the role of HDACs activity on the chemosensitivity of CML cells and suggested panobinostat as an appealing agent in CML treatment strategies.

Keywords: CML; Histone deacetylase (HDAC); HDAC inhibition; Panobinostat

Abrogation of histone deacetylases (HDACs) using Panobinostat increased the sensitivity of chronic chronic myeloid leukemia cells to Imatinib (Research Paper)

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Introduction: Although tyrosine kinase inhibitors (TKIs) improved the treatment process of CML, approximately 30% of patients resist TKIs especially in the accelerated and blast crisis phases of the disease. The acquired escape mutations in the kinase domain of BCR/ABL are the main cause of resistance to the first-line TKI (imatinib). Apart from resistance to TKIs that is mediated mainly by BCR/ABL mutations, a subpopulation of leukemic stem cells may exist in the bone marrow, serving as an alternative source of disease relapse. A mounting body of evidence declared that abnormal epigenetic mechanisms through changing the expression and activity of either HATs or HDACs could disrupt the balance between acetylation and deacetylation of histone or non-histone proteins and thereby endows cancer cells with an abnormal advantage of excessive proliferation.

Methods: In order to evaluate the effect of Panobinostat with Imatinib on CML cells, K562 cells were cultured in RPMI 1640 medium and they were treated with inhibitors. Then cell survival was evaluated using Trypan blue exclusion assay and MTT assay. Apoptotic property of panobinostat-plus-imatinib determined using Annexin V/PI staining.

Results: Treatment with the combination of panobinostat and imatinib, as the first-line tyrosine kinase inhibitor used in CML treatment, was further effective in suppressing cell viability and metabolic activity as compared with either drug alone. The results of the annexin-V binding assay also revealed that the cytotoxic activity of panobinostat-plus-imatinib is mediated through the induction of apoptotic cell death

Conclusion: Due to the pharmacologic safety of panobinostat, our study suggests the beneficial application of this inhibitor in the treatment strategies of CML, either as a single agent or in combination with small molecule inhibitors of oncogenic pathways.

Keywords: Chronic myeloid leukemia; Histone deacetylase (HDAC); HDAC inhibition; Panobinostat; Imatinib;

Acetylation of lysin and N termini residues of human insulin: study on structural alterations (Research Paper)

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Introduction: Acetylation is one of the major post-translation protein modification in the cells, with manifold effects at protein as well as the metabolome level. While acetylation may affect the structure of proteins and their subsequent aggregation, the consequences of aggregates formation are very important for pharmaceutical biologics such as insulinb [1,2].

Methods: In the present work, molecular dynamics simulation experiments, have been performed on native and acetylated forms of human insulin. Acetyl groups were added to GlyA1, PheB1 and LysB29 of the A and B chain, of insulin respectively). Three temperature of 37°C, 50°C and 100°C were used and both neutral and acidic pH environments effects were applied to. Molecular dynamic, MD, study was done in YASARA (17.3.30) for 3x-100ns MD simulations in NPT ensemble and using Amber 14 force field.

Results: The results showed that acetylation causes structural changes of insulin molecules which were accompanied with increase in protein surface hydrophobicity, and change in the secondary structure content (e.g. alpha-helix to beta –sheet transition which could be indicative of aggregation propensity) but this structural changes vary in different types of acetylated insulin. According to the data of RMSD, most changes related to acetylated forms of insulin in PheB1 and LysB29 of B chain also analysis of the secondary structure shows that the acetylated forms of insulin in PheB1 and LysB29 of B chain have the lowest content of beta-sheet in their structure. Acetylated insulin is less constrained geometrically and, as a result, more openly packed than native insulin[3,4].

Conclusion: The optimization of these modified insulin forms can lead to a better stabilized form of insulin and be potentially useful for the development of new therapeutic purposes with applied vision in the developing world.

Keywords: Insulin, lysin acetylation, Molecular dynamic, Simulation, Protein aggregation.

Acinetobacter baumannii : Evolution as an opportunistic nosocomial and successful pathogen worldwide (Review)

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Introduction: Gram-negative coccobacilli classified as Acinetobacter baumannii are important Gram-negative opportunistic bacterial pathogens that are responsible for 2–10% of all Gramnegative hospital infections(Joly-Guillou, 2005; Khadke et al., 2019). Acinetobacter baumannii infections have become an emerging health concern in hospitals across the world and are often associated with nosocomial infections with poorer clinical outcomes in patients with prolonged hospital stay(Nasr, 2020). Acinetobacter baumannii has been recognized as an agent of pneumonia, septicemia, meningitis, urinary tract and wound infections, and is associated with high mortality(Ayoub Moubareck & Hammoudi Halat, 2020). Acinetobacter baumannii is classified by the Infectious Diseases Society of America as one of the six most important multidrug-resistant (MDR) microorganisms in hospitals worldwide (Luısa et al., 2014). Indeed, the World Health Organization (WHO) has recently identified antimicrobial resistance as one of the three most important problems facing human health (Howard ,A. et al., 2012). The WHO has stated Acinetobacter baumannii to be one of the most serious ESKAPE organisms(Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp) that have effectively escaped the effects of antibiotics(Mujawar et al., 2020). The Infectious Diseases Society of America (ISDA) stated Acinetobacter baumannii as one of the “red alert” pathogens that greatly threatens the utility of our current antibacterial armamentarium (Yadav et al., 2020). The aim of this mini-review summarises these recent advances, with particular focus on multidrug-resistance of Acinetobacter baumannii, and proposes new avenues of research.

Methods: This is a descriptive study. In this review summarise recent advances in knowledge concerning Acinetobacter baumannii, with particular focus on the multidrug-resistance of Acinetobacter baumannii pathogenicity, it should also be considered that the nature of the host (i.e. human patient) may also play a large part in the outcome of infections caused by Acinetobacter baumannii.

Results: The majority of Acinetobacter baumannii infections are caused by two main population clones with worldwide distribution. Infection outbreaks are often associated with multidrug resistance, including the recent emergence of strains resistant to all available antibiotics.

Conclusion: Acinetobacter baumannii virulence traits and pathogenic potential have mostly remained elusive. Acinetobacter has been known as a major cause of

nosocomial infections worldwide and have shown a broad spectrum of resistance toward commonly used antimicrobial agents. Acinetobacter baumannii has evolved as a hospital pathogen, due in part to excessive and inappropriate use of antibiotics. Its transmission has been associated with war, natural disasters, and just about any other instance where one observes an influx in hospital trauma admissions and increased transfer of patients and staff from one hospital to the next. Patients infected with a clinical isolate of Acinetobacter baumannii have an average of $60,913 in additional patient charges due to the infection, and they stay in the hospital for an average of 13 days longer than a patient without an Acinetobacter baumannii infection. While Acinetobacter baumannii may not be particularly virulent, it can cause unnecessary disease and expense in the critically ill patients affected by it, and the transmission of such a pathogen should be limited. Measures to prevent the inter- and intrahospital transmission of Acinetobacter baumannii must be established in health care settings. Success in infection control has been attained by numerous others, and it can be attained by all if health care workers are educated about the proper way to manage MDR Acinetobacter baumannii. researchers understanding of the role of combination therapy for patients with multidrug or pandrug-resistant Acinetobacter baumannii infections is also critical. New therapeutics are clearly needed, and we as clinicians, microbiologists, and scientists must think broadly about our approach to antimicrobial drug development, as novel targets will no doubt provide the most reward for our afflicted patients. This review summarises these recent advances, with particular focus on Acinetobacter baumannii multidrug-resistance, and proposes new avenues of research.

Keywords: Acinetobacter baumannii, multidrug-resistant (MDR) microorganisms, hospital infections

Advance in Drug Delivery Nanosystem For Cancer Therapy (Review)

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Introduction: Many chemotherapy drugs have adverse effects that can be severe. The main adduction of chemotherapy are its extravagant bioavailability, high-dose prescriptions, adverse side effects, low therapeutic roster, development of manifold drug resistance, and non- exclusive targeting

Methods: however conventional chemotherapy has been triumphant to some vastity The essential aim in the development of drug delivery carriers is to successfully token these delivery-related problems and carry drugs to the eligible sites of therapeutic operation while decreasing detrimental side effects

Results: In this review, our research bring up the various particles of materials operated as delivery transport for chemotherapeutic factors and their structural specification that ameliorate the therapeutic influency of their drugs

Conclusion: and information offered will process new understanding into the communicative usage of Drug Delivery nanosystem in cancer therapy.

Keywords: Nanosystem, Drug Delivery, Cancer, Chemotherapy.

Algae and Fungi; the bioreactors for pharmaceutical s removal (Review)

soha mokhtari garakani,[1,*] Shima Mokhtari Garakani,[2]

1.
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Introduction: Todays, water pollutions put human health in danger and with the population increasing, these dangers have become more and more considerable. Furthermore, pharmaceuticals contamination has become more widespread and diverse. Therefore, Water treatment is an urgent concept in our world. The suitable methods with low operation Costs, easy operation, proper investment and the non-formation of degradation by-products -as features- are gathering in algae and fungi as suitable bioreactors.

Methods: the increasing pharmaceuticals consumption which cause aquatic ecosystems pollutions is our recent decade problem. wastewater treatment plants (WWTPs) were unable to remove pharmaceuticals completely. Fortunately, the treatments achieved by Fungi and algae performance are eco-friendly promising technologies for suitable treatments.

Results: bioremediation is a bio treatment in which the microorganisms have the main role through the processes. Through the different study about organic compounds bioremediation steps dependent on environmental, physical and chemical factors. Though bioremediation is a proven method but insufficiency about some compounds removing shows our requirement to genetically modified microorganisms. fungi fungi, which are categorized as eukaryotic organisms, one of our mycoremediation tools. They known as recalcitrant compounds transformers which using nonspecific intracellular and extracellular oxidative enzymes, also can tolerate the sudden changes in pH or humidity because of their Mycelium physiology and colonization strategy. though long growth cycle and spore formation are their limitation. fungi can have suspended growth or immobilized systems and the second one have the fast biodegradation. also their growth condition can be under aerobic or anaerobic conditions. Fungi are as bio reactors or mycoreactors can be active in batch, semi-batch, sequencing batch, or continuous mode. White-rot fungi (WRF) belong to Basidiomycota phylum which are filamentous wood-degrading fungi and one of the most important fungi studied that can help us in lignin mineralization and help us to recalcitrant pollutants degradation. Both intracellular enzymatic system (i.e., cytochrome P450 system) or an extracellular enzymatic system (mainly lignin peroxidase, manganese peroxidase, laccase, and versatile peroxidase) help WRF to have proper degradation. In many cases, there would be the preference to use isolated enzymes (enzymatic bioremediation) than fungi biomass to reduce treatment time fungal growth period, to reduce sludge production, and to facilitate process control. Algae Algae are categorized as both prokaryotic and eukaryotic organisms and most of them are in microscopic size. autotrophcation, heterotrophication and mixotrophication energy cycle producing Of Algae are their supremacy. and living in harsh environmental conditions like low nutrient levels, and extreme pH and temperature tolerance are their species advantage Properties. Algae haven’t shown successful results during their

Individual Activity. but in the companion of bacteria the results changed upside down and all biodegradation, biomineralization (bioprecipitation), biosorption (cell adsorption and/or bioaccumulation), stripping (volatilization), and photodegradation processes come to gather due to light effect. In many cases, the complete removal of the pharmaceuticals requires the microorganisms several group interactions which is involve with degradation phase. The alga such as Anabaena cylindrica, Chlorococcus, Spirulina platensis, Chlorella, Scenedesmus quadricauda, and Anaebena in companion of duckweed such as Lemna was successful bioreactor for pharmaceutical removing. This collection was successful especially for the compounds like synthetic hormone 17α-ethinylestradiol, natural hormones estrone and 17β-est even in low concentration levels.

Conclusion: The wastewater treatment industry faces widespread problems, including pharmaceutical pollution Which develop our approach to wastewater treatment. We tried to have short overview about fungi and algae potentials in pharmaceuticals removing bioremediation and bio absorption processes. Algae exhibit considerable advantages in compared by fungi, such as fast growth though both group are successful in pharmaceutical removing. In fact, there are a few Practical studies available and there would be a long way in this field for the future to understand the complexity of the processes, their dependence on physical and chemical factors, and the involved mechanisms. Furthermore, we have to received proper help from genetic engineering knowledge to have metabolic genes key to produce and amplify new effective algae or fungi strains. Absolutely applying new strains need to consider about legal limitations, as well as marketing challenges and consumption costs.

Keywords: algae; fungi; pharmaceuticals; bioremediation

Allelochemical therapeutic properties as natural bio-active compounds: A pharmacological approach (Review)

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Introduction: The nature is the major source of natural compounds with potential in pharmacognosy. In particular, during the last few decades, allelochemicals that are produced chiefly by plants, bacteria, fungi, lichens, micro- and macro-algae, viruses, and even animals have been in focus as interesting bioactive compounds, especially for the treatment of cancer. Allelochemicals are species- and tissue-specific compounds, mainly producing as secondary metabolites and are known as responsible compounds in allelopathic interactions. In addition, these compounds can release due to decomposition of organic materials by microbes.

Methods: The current review focuses on introduce and classification of the allelochemicals and their therapeutic properties and sources. This review provides an opportunity to reveal a relationship between allelopathy phenomenon and diseases managements in the ecosystems specially allelochemicals potential in human's diseases remedy.

Results: Accurate assessment of literatures showed that the allelochemicals sources and features are very different and some compounds have an excellent therapeutic effects in comparison to the others than. Although these multifunctional interesting compounds were evolved in the organisms especially against biotic stresses, but they are also used in the treatment of non-contagious and physical diseases such as heart disease, which can be used as smart strategy in controlling of human's diseases. There are numerous examples of allelopathic compounds with terrestrial and marine organisms' origins that promise to incurable diseases remedy. One of the most ancient applications of allelochemicals is the use of Digitalis and Diosgenin to treat cardiovascular disease. The most well-known examples of allelochemicals utilization are related to the cancer treatment including Taxol and Vinblastine, and recently Curcumine. Chloroquine for malaria treatment, Colchicine for gout and Behçet's disease, Batatasin for diabetes, the majority of volatile allelochemicals such as Pinene, Cineole, and Eucalyptol in aromatherapy for non-purulent rhinosinusitis, Benzoxazinones for preterm labor, Rosmarinic acid for asthma and alzheimer's disease, Thymol and its isomer Carvacrol for respiratory disorders and skin infection diseases are the simple samples of allelochemicals utilization as human's diseases remedy worldwide. The most recently study of Chinese scientist's shows that allelochemicals including Baicalin, Scutellarin, Hesperetin, Nicotianamine, and Glycyrrhizin that their therapeutic properties have been identified previously in the treatment of SARS, are the good herbal options for

Covid-19 remedy. This study further reveals the value of investing in allelopathic compounds.

Conclusion: With increasing reliance on herbal medicine and natural remedy power, increasing attention has been paid to allelopathy research in the pharmacology, and the molecular mechanisms of allelochemicals that underlie its therapeutic effects are gradually being elucidated as well. It is clear that allelopathy requires advanced techniques and more research for widespread application in pharmaceutical industry worldwide; however, its first steps have been unintentionally taken.

Keywords: Allelochemical, therapeutic properties, allelopathy, pharmacognosy

An overview of allergy prevention in breastfed infants (Review)

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Introduction: Today, atopic diseases and food allergies are on the rise around the world and it is considered as one of the health problems. Food allergies are defined as an adverse immune response to food and it happens when the immune system responds to harmless proteins. That is, it cannot recognize them and think of them as pathogens. Because food allergies can be life threatening and children with food allergies are more likely to develop asthma or respiratory allergies, Therefore, food allergies must be taken seriously.

Methods: Data from the present study by searching databases" Google scholar, SID, Magiran, Clinicalkey, ScienceDirect " gathered and After extracting the materials related to the subject, they were analyzed.

Results: Exclusive breastfeeding reduces the risk of respiratory attacks, asthma, Skin allergies and eczema in in 27% of normal infants and 42% of infants with a family history. Insulin in breast milk causes premature infant's intestines development and decreased permeability to macromolecules that it plays an important role in preventing allergies and the development of the infant's immune system. Feeding a baby with cow's milk or artificial milk increases the IgG antibody titer and breastfeeding delays IgG production compared to cow's milk. Starting a complementary diet after 6 months has no effect on allergies, but foods like cow's milk, soy, eggs, fish if present in the mother's diet, it can cause allergies in infants.

Conclusion: Breastfeeding can strengthen the immune system and prevent food allergies as well as wider allergic reactions such as asthma , The anti-allergic effects of breast milk are evident even in adolescence and adulthood. Because breast milk can prevent one of the most serious forms of allergies, respiratory allergies and asthma, reduces treatment and hospitalization costs.

Keywords: Breastfeeding, Allergy, Prevention, Infants.

An overview of emerging infectious diseases (Review)

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Introduction: The third outbreak of coronavirus, which started in 2019 in China and affected more than 160 countries. This epidemic underscores the importance of paying attention to emerging infectious diseases. The purpose of this article is to review the emerging infectious diseases, their importance and ways to deal with them.

Methods: This review study is combined with the author's personal experience by referring to authoritative domestic and international sources.

Results: The most important ways to deal with emerging and new diseases; Support the system of active care of infectious diseases, strengthen communication and cooperation with national and international institutions, expand antimicrobial susceptibility testing, improve diagnostic capabilities to identify pathogens, increase the number of skilled personnel, expand applied research, expand reporting Accurate and timely cases of diseases at the national and international levels and the widespread use of antimicrobial drugs by the medical community.

Conclusion: Monitoring, rapid diagnosis of the prevalence of emerging infectious diseases, requires policy-making, education, planning, support and responsible actions of countries and health systems. These, in turn, owe their existence to a robust, flexible and intelligent health system. WHO Strategies for Combating Coronavirus Pandemic: Breaking the human-to-human transmission chain that reduces secondary infections and prevents the spread of transmission and prevents the spread, early detection and diagnosis, for example, optimal care of infected patients, reporting of risk and disease events, and finally addressing important unknowns about disease and prevalence. Transmission of infection and treatment and vaccines.

Keywords: Emerging diseases, Recurrent diseases, Ebola, Corona virus

An overview of MAD2 protein, its functions and its association with Cancer (Review)

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Introduction: The spindle assembly checkpoint (SAC) involves the MAD proteins; MAD1, MAD2, BUBR1 (MAD3), and BUB1. The Mitotic-arrest deficiency 2 (MAD2) is a key component of SAC function and controls cell entry from the metaphase to the anaphase stage. MAD2 are located in spindle poles, kinetochores and cytoplasm of early prometaphase LLC-Pk cells and capable of heterodimerization and thereby recruits free MAD2 from the cytosol. The MAD2 gene was first discovered in the yeast Saccharomyces cerevisiae and also is present in most kinetochores in the first meiotic division and remains associated with the kinetochore throughout MI. It does not dissociate during metaphase and anaphase, as is the case for mitosis. The human orthologues of this protein are MAD2L1 and MAD2L2. MAD2L1 and MAD2L2 gene related to each other and located on chromosome 1.

Methods: Articles related to the subject were searched on two sites of Science Direct and Google scholar, and 25 articles that examined MAD2 protein and its association with Cancer were included in the study.

Results: The entry from metaphase to anaphase is accomplished by the separation of sister chromatids. The cell cycle regulatory mechanism that prevents these chromatids from being separated is called the spindle checkpoint, which has a protective role against chromosomal aberrations and MAD2 has a prominent role in this process. The size of MAD2 is 25 kDa and consists of two parts with different features called Open-MAD2 (O-MAD2) and Closed-MAD2 (C-MAD2). Kinetochores devoid of microtubules maintain a tight complex of MAD2 with another SAC protein named Mad1. Binding of MAD1 to MAD2 leads to a complex that acts as a template for MAD2 activity and binds to Cdc20. The MAD2 binding site to Cdc20 is held in a binding pocket of MAD2 by a mobile element called the “safety belt”. This interaction is essential for SAC function. Disruption of MAD2 expression can cause various cancers, including ovarian, colorectal, breast, bladder, lung and etc. In the recent years, researchers inquire the treatment of cancer based on the selective killing of mitotic checkpoint competent cells, and assay the effect of MAD2 expression on cellular sensitivity to checkpoint-targeting anticancer drugs. However, studies have shown that different ovarian cancer subtypes exhibit different expressions of MAD2. There is no strong evidence that low levels of MAD2 expression cause recurrence of cancer. As expected, elevated levels of MAD2 expression are directly associated with increased chances of surviving ovarian cancer patients but is different from other types of cancers. In ovarian and breast cancers, it has been found that the P53 and BRCA1 genes are responsible for regulating MAD2 expression. In addition, research has shown that silencing of the MAD2 gene by siRNAs can be one of the therapeutic approaches in ovarian cancer cases. In some sort of the lung cancer (NSCLC), MAD2 overexpression has been observed in most cases. It also appears that patients with tumors with MAD2

overexpression have a shorter life expectancy. Significant increases in MAD2 expression can also be observed in colorectal cancer and bladder cancer. On the other hand, in cases of gastric cancer, there was a significant increase in MAD2 expression compared to normal tissues.

Conclusion: MAD2 expression as a prognostic marker for human malignant cancers and according to research and observations, we can find that MAD2 increases in some types of cancers and decreases in others and is one of the important factors in regulating the cell cycle. In fact, it can be said that alterations in the expression of this protein can lead to cancer awareness. Consequently, prophylactic medications may be used instead of chemotherapy after cancer. However, according to available studies, further studies are needed to understand the exact mechanism of this disease.

Keywords: MAD2, Spindle assembly checkpoint, Cancer

An Overview of Novel Corona Virus Disease (Covid-19) (Review)

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Introduction: 2019-nCoV is the third coronavirus to cross species to infect human populations in the past two decades. The previous two coronavirus are the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012. The world has seen the onset of a pandemic of a new infectious disease from December 2019. This has been formally named as the CoronaVirus Infectious Disease (COVID)-19 by a consensus group of WHO experts. Numerous clusters of patients started to surface in Wuhan, Hubei Province, China in mid December 2019. They presented with features of a viral respiratory illness with complaints of fever, cough, headache and breathlessness. Some of the patients had evidence of respiratory failure, shock, acute respiratory distress syndrome (ARDS) and sepsis. Laboratory tests were not detection various respiratory viruses, bacteria or fungal pathogens. A genome sequencing of the respiratory tract samples from these pneumonia patients ultimately led to the isolation of a new novel beta-coronavirus which was initially called “Wuhan virus”, novel coronavirus (nCoV-2019) and later severe acute respiratory syndrome (SARS)-2 coronavirus.

Methods: The confirmation of clinical diagnosis for COVID-19 can be done by certain laboratory tests. WHO released its interim guidelines for laboratory biosafety and prioritized laboratory testing strategy on 19 and 22 March 2020. Real-Time Reverse transcriptase (RT)-Polymerase chain reaction (PCR) is used for detection of virus. Various biological samples like nasopharyngeal swabs/washes/ aspirates, sputum, BAL etc. can be tested for the presence of virus. Gene targets in N gene, ORF1ab, nucleoprotein, RdRP, spike protein have been used for detection of the virus. Presently various commercial kits for detection of the virus have been validated. They employ these targets for detection of the virus by real time reverse transcription polymerase chain reaction (RT_PCR). In 2nd or 3rd week of illness, various antibodies have been detected in the convalescent serum of the donors. 32 Rapid diagnostic test kits have been recently developed. They can detect the SARS-CoV-2 in few hours and can be used as screening tests in certain hot-spot areas of the epidemic. These tests have an accuracy of 95% for detection of infection (nasal/throat swabs) and meet various quality control standards as per WHO. They can be used at various points of patient care and no transportation of samples is required. However the test results by these rapid diagnostic kits need to be confirmed by RT-PCR for SARS-CoV-2

Results: Both SARS-CoV and SARS-CoV-2 are CoVs; hence, the treatment strategies of SARS could be relevant for COVID-19. In 2003, SARS was mainly

treated by isolation of the patients, hormones treatment, antiviral and symptomatic treatments, and many drugs such as glucocorticoid and interferon.Now, isolation, antiviral, and symptomatic treatments are still mainly adopted for COVID-19 treatment. As effective drugs for SARS, hormones and interferons can also be used to treat COVID-19. Lopinavir is one kind of protease inhibitor used to treat HIV infection, with ritonavir as a booster. Lopinavir and/or ritonavir has anti coronavirus activity in vitro. Hong Kong scholars found that, compared with ribavirin alone, patients treated with lopinavir/ritonavir and ribavirin had lower risk of acute respiratory distress syndrome (ARDS) or death caused by SARS-CoV. Lopinavir/ritonavir has also been clinically tested in treatment of COVID-19, and showed wonderfully effective treatment for some patients, but the general clinical effect has not been determined . More effective treatments are still under continuing exploration.The first patient in the US had been trial-treated with intravenous remdesivir (a novel nucleotide analogue prodrug in development) due to a severe infection. No adverse reactions were observed during the administration, and the patient's condition was effectively improved.

Conclusion: Coronavirus infections have lead to few epidemics and a new pandemic in last 2 decades. The infections vary in clinical manifestations from self limiting viral respiratory tract infections or gastroenteritis to severe form like the SARS-CoV-1, MERS and the recent SARS-CoV-2 infections. These have led to a significant morbidity and mortality and a global economic crisis. Newer developments in therapeutics, preventive therapy in the form of chemoprophylaxis and vaccines are underway. Newer information about the molecular mechanisms, clinical manifestations, epidemiological pattern and preventive public measures is available each week in all the scientific or medical journals.

Keywords: Acute Respiratory Syndrome-Corona Virus-Lungs-Sars-Cov2-ORF1lab

An overview of the coronavirus biology and its specific receptors (Review)

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Introduction: Introduction: Recently, the global epidemic of Covid19, which is caused by acute respiratory syndrome (SARS-COV-2), is spreading widely around the world. (SARS-COV-2) is a positive single-stranded RNA virus that can infect the respiratory tract and respiratory tract. The virus has at least four structural proteins protected throughout COV: Spike (S) protein, membrane protein (M), an envelope protein (E), and nucleocapsid protein (N). The Spike protein is responsible for binding to host cell receptors and entering the virus. Research to date on the new coronavirus has shown that the receptor (ACE2) is the major receptor for the virus, which has been shown to be on the outer membrane of the main cells of the lung, heart, kidney, arteries, and intestine. In addition to the receptor (ACE2), there is another membrane protein called CD147, which is a membrane-wide glycoprotein that can be used as a gene pass for coronavirus. Using molecular modeling methods and the results of bioinformatics studies, the researchers also found a structure to which Spike protein could be attached, called the Glucose Regulated Protein 78 (GRP78).

Methods: Method: In this study, we collected information by reviewing several articles and current sources in the world.

Results: Results: There are now widespread global concerns about the coronavirus SARS-CoV-2 crisis that originated in China, and it is important that we understand the biology of the virus and its surface proteins and specific receptors, how and by what mechanism the virus becomes more common with target cells.

Conclusion: Conclusion: This strategy makes us more efficient in defending against this virus, so providing existing and new information in the form of compiling and publishing review articles to teach and increase awareness and transfer important scientific concepts for the next generation. Recommended and in principle, the article has considered this important goal.

Keywords: Keywords: Covid19, Severe Acute Respiratory Syndrome, ACE2, CD147, GRP78, Surface Proteins

An Overview of the Taxol Anti-Cancer drug, Its Biosynthetic Pathway, Extraction, and its Mechanism on Cancer Cells (Review)

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Introduction: Medicinal herbs make up more than 25% of the world's total medicines, which play a special role in providing anticancer drugs. That Taxol and its constituents (Taxanes) or (Taxoid) are of great importance. Taxol is a de-terpenoids alkaloid approved for use in the treatment breast, ovarian and lung cancers as well as AIDS-associated Kaposi's sarcoma. Recent research has shown that hazelnut and its cellular properties also produce detaxan components, including Taxol. In addition, the efficacy of these drugs in other diseases, including polycystic liver disease and Alzheimer's, has been proven in many studies and clinical trials. Taxanes are secondary metabolites and diterpene compounds that protect the plant against wounds and plant pathogens. The accumulation of secondary metabolites in plants is part of the immune response to pathogenic attacks induced and activated by stimuli. Stimulants commonly used in studies include fungal carbohydrates, yeast extract, methyl jasmonate (MJ), salicylic acid, and Chitosan. The natural source of taxons is a species of yew tree. Yew (Taxus baccata) is a coniferous tree that is a living legend and the masterpiece of northern Iran's forests since the third geology.

Methods: Articles related to the subject were searched on two sites of Science Direct and Google scholar, and 24 articles that examined the Taxol Anticancer drug, Its Biosynthetic Pathway, Extraction, and its Mechanism on Cancer Cells were included in the study.

Results: Despite many efforts to identify the biosynthetic pathway of Taxol, a clear and precise conception of it is still not available. High diversity of taxon compounds and their similarity to each other, low concentrations of intermediate compounds and many metabolic stages are the most important barriers to the recognition of this biosynthetic pathway. However, researchers using a combination of biochemical and genetic techniques and have succeeded in providing a relatively clear idea of this biosynthetic pathway. Due to its scarcity, slow growth and very low concentration in the natural plant, as well as the presence of more than 400 similar compounds that make the purification process very complicated, extraction of these materials from the plant is not a cost-effective method and has been replaced by other methods. Chemical synthesis, semi-synthesis, and microbial production are some of the methods commonly used to replace previous methods, but very low yields due to the production of many undesirable isomers, large fluctuations in precursor production and very low production compared to the plant itself. The most important problems with these methods are. Nowadays, plant cell culture is recognized as one of the alternatives and reproducible sources for the production of secondary metabolites. The exact mechanism of Taxol for cytotoxicity against tumor cells is not completely clear. Taxol inhibits microtubule depolymerization and promotes the formation of highly stable microtubules, thereby disrupting the normal dynamic reorganization of the microtubule network required for mitosis and cell

proliferation. Taxol drives inactive GDP-tubulin into microtubules, replacing the need of the g-phosphate of GTP to activate the protein. Taxol stabilizes microtubules by binding preferentially to assemble tubulin with an exact 1:1 stoichiometric ratio. Unpolymerized tubulin has no significant affinity for Taxol, indicating that the binding site is formed during the polymerization process. Another Taxol's therapeutic feature is high effect in inducing cell cycle arrest in human glioblastoma cells. One more mechanism of Taxol is Induction of Apoptosis. Apoptosis, the terminal point of programmed cell death, is well characterized by morphological and biochemical features. Several lines of evidence from recent studies have suggested that Taxol induces apoptosis through a signaling mechanism independent of microtubule and mitotic arrest. Taxol is highly effective in inducing cell cycle arrest in human glioblastoma cells.

Conclusion: As mentioned, there is some difficulty in extracting this material, however, understanding the expression and expression level of different genes and identifying the key genes involved in Taxol biosynthesis can guide us in directing Taxol biosynthetic pathway genes in yew. Also, because the Taxol biosynthesis pathway has not been fully identified, studying gene expression patterns and proteomics analysis could be helpful in helping to better treat cancer.

Keywords: Taxol, Cancer, Anticancer drug

Angiogenesis inhibition improves asthmatic attacks (Research Paper)

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Introduction: Studies on the bronchial vascular bed revealed that an amount of blood vessels in lamina propria and submucosa of the lung tissue in patients who suffered from mild and severe bronchial asthma. So, in this study, a new strategy was used in respiratory system disorders by angiogenesis inhibition in an ovalbumin-induced rat model of asthma.

Methods: Twenty one male Wistar albino rats, 8 weeks old, weighing between 250 and 300 gr were randomly divided into three groups (n= 7 in each) including (1) Control group, (2) OVA-treated group and (3) OVA + Avastin (Avastin drug). On days 1 and 8, 1 mg of OVA and 200 g of aluminum hydroxide in 0.5 mL sterile phosphate-buffered saline (PBS) were intraperitoneally injected to rats in groups 2 and 3. The control group were only subject to intraperitoneal injection of saline on day 1 and day 7. One week after the last injection, the rats (groups 2 and 3) were exposed to OVA inhalation for 30 min at 2-day intervals from days 15 to 25. After preparation of asthma rat models through OVA exposure protocols, the OVA+Avastin group (group 3) were treated with5 mg/kg Avastin drug.

Results: Genes and proteins expression of cytokines in lung tissue and the expression of VEGF protein were assessed in lung tissue. Ovalbumin exposure increased mucosal secretion and VEGF expression and expression of cytokine factors ($p \leq 0.05$). However, rats in OVA+Avastin group showed significantly decrease in VEGF and IL-1β and TNF-α genes and proteins ($p \leq 0.05$).

Conclusion: The results showed that Avastin efficiently eliminated bronchial inflammation via down regulation of VEGF expression, followed by inflammatory cytokines reducing.

Keywords: Avastin; Asthmatic attacks; IL-1β; TNF-α

Anti-oxidant, anti-bacterial, and anti-fungi potential of redroot pigweed's allelochemicals (Research Paper)

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Introduction: Redroot pigweed (Amaranthus retroflexus L.) is a weed plant with well-known allelopathic effects worldwide. Its allelochemicals belongs to different groups of plants secondary matabolites. Dom which some compounds such 5 alpha pregnane, carvacrol, thymol, and sabinene have therapeutic effects. Interestingly, the majority of these allelochemicals are the excellent anti-oxidant compounds as well. Current research aimed to assessment the anti-bacterial and anti-fungal potential of redroot pigweed's allelochemicals and subsequently evaluation its anti-oxidant capacity.

Methods: In order to, MIC (at different concentration including 1000, 500, 250, 125, 62.5, 31.25, 15.6, and 7.81 µl/ml) and DPPH assay with estimation total phenolics, flavonoids, and anthocyanins were used. Strains that used in this research were including combination of gram-positive, gram-negative bacteria and saccharomycete fungi.

Results: The redroot pigweed's allelochemicals showed an excellent anti-bacterial effect on gram-positive bacteria and Candida fungi, but they have less effective on gram-negative bacteria and can be considered as candidates in the anti-biotics production for gram-positive bacteria especially S.aureus and S.epidermidis and Candida fungi. DPPH assay revealed that amaranth allelochemicals inhibit the superoxide radical production in a dose-dependent manner and 400µg/ml of allelochemical's extract showed the highest free radical scavenging activity (87.35%). Total phenols, flavonoids, and anthocyanins contents of this extract were 4.81, 1.56 and 0.52 mg/g DW, respectively. Therefore, based on the literature, total phenolics, flavonoids, and anthocyanins contents of redroot pigweed extract were in the moderately level. But, according to the DPPH assay results, probably other anti-oxidant metabolites such terpenoid compounds were involving in the free radicals scavenging. GC-MS analysis results of redroot pigweed's allelochemicals profile supported this interpretation.

Conclusion: Redroot pigweed is one of the most invasive weed worldwide that reduce crops yield. Yearly, large quantities of poisons are used as herbicides to combat whit this weed. Apart from the economic costs of production, these compounds are toxic substances that impose irreparable effects on the

environment and are also hazardous to humans and livestock. Therefore, using this plant to produce medicines can reduce the environmental damage. According to the literature using allelochemicals derived from the various organisms as anti-bacterial and anti-cancer agents are increased day-by-day and this event represents the most promising to application of amaranth allelochemicals as an anti-biotics.

Keywords: Anti-bacterial, anti-oxidant, anti-fungi, redroot pigweed, DPPH assay

Antibacterial activity of nickel and nickel hydroxide nanoparticles against multidrug resistance E. coli isolated urinary tract (Research Paper)

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Introduction: Antibacterial materials are so significant in the textile industry, water disinfection, medicine, and food packaging. Unfortunately, organic compounds for sterilization show toxicity to the human body; therefore, the interest in inorganic disinfectants such as metal oxide nanoparticles (NPs) is increasing.

Methods: Nickel and nickel hydroxide nanoparticles (NiNPs and Ni(OH)2-NPs) were prepared and characterized by DLS, SEM, AFM and ATR. Antibacterial activity assay was carried by Spot on lawn method against two selected standard pathogenic bacteria such as E. coli (as Gram negative), S. aureus (as Gram positive) and multidrug resistance E. coli. Also the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined against two selected standard pathogenic bacteria and multidrug resistance E. coli.

Results: The formation of the NiNPs and Ni(OH)2-NPs were confirmed by DLS, SEM, AFM and ATR. Antibacterial activity of nanoparticles were confirmed against two selected standard pathogenic bacteria such as E. coli and S. aureus. And also, NiNPs and Ni(OH)2-NPs revealed fair antibacterial effect against multidrug resistance E. coli based on MIC and MBC data. As well, the experimental data presented that the antibacterial activity of NiNPs was more than Ni(OH)2-NPs.

Conclusion: Based on the achieved results, NiNPs and Ni(OH)2-NPs show antibacterial activity against clinical patients bacteria (multidrug resistance E. coli(. Finally, the NPs evaluated in this study have promising properties for applications as antiseptic agent for environment; however, further studies are warranted such as study toxicity NPs on normal human cell line and other clinical bacteria.

Keywords: Antibacteial, NiNPs, Ni(OH)2, Nanoparticles, Pathogen

Antibacterial activity of zinc oxide nanoparticles on Escherichia coli (Research Paper)

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Introduction: Antibacterial activity of zinc oxide nanoparticles (ZnO-NPs) has received significant interest worldwide particularly by the implementation of nanotechnology to synthesize particles in the nanometer region. Many microorganisms exist in the range from hundreds of nanometers to tens of micrometres. ZnO-NPs exhibit attractive antibacterial properties due to increased specific surface area as the reduced particle size leading to enhanced particle surface reactivity. The present study was aimed to explore the antibacterial effects of ZnO NPs on E.Coli O157: H7.

Methods: In this study, The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of nanoparticles of zinc oxide were determined using well assay method.

Results: According to the results of this study, the MIC values of ZnO nanoparticles for this bacterium were 4 mg/ml and the MBC values for Escherichia coli isolate were 8 and 4 mg/ml, respectively.

Conclusion: The present study showed that zinc oxide nanoparticles can be used as a deterrent against the pathogens of the materials and avoid contamination. Finally, the results obtained in this study suggest that the use of ZnO-NPs as an antibacterial agent in food systems can successfully inhibit some of the most dangerous and frequent foodborne pathogens.

Keywords: Nanoparticle, Zinc Oxide, Escherichia coli, Antibacterial

Antibacterial Effects of Essential Oil of Hedge Nettle and Purslane Plants 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 causes of nosocomial infections and multi drug 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. On the other hand, medical properties of the extracts and essential oils against microbial as well as non microbial diseases have been known since ancient times and many studies have been performed on medical properties of the different plant species and their essential oil or extracts effects on microorganisms.

Methods: In this study, essential oil was prepared from dried leaves of the Stachys schtschegleevi and Portulaca oleracea, 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 intrapertioneally injected. Then, the counting of bacterial clonies 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 Stachys schtschegleevi (30 mm), and the minimum of growth inhibition diameter is related to essential oil of Portulaca oleracea (10 mm) at the highest concentration (400 mg/ml). The results of broth microdilution method on Staphylococcus aureus showed that the amounts of the MIC and MBC in essential oils of the Stachys schtschegleevi and Portulaca oleracea were the same and equal to 3.90 mg/ml and 7.181 mg/ml. any antimicrobial activity. In conditions of in vivo, spleen supernatant cultivation, the average number of bacteria for Stachys schtschegleevi and Portulaca oleracea 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 Stachys schtschegleevi and Portulaca oleracea have the effective antibacterial activity against mentioned bacteria and can be useful to treatment of nosocomial infections.

Keywords: Antimicrobial, Essential oil, Portulaca oleracea, Stachys schtschegleevi, Staphylococcus aureus

Antibacterial Effects of Extract of Hedge Nettle and Purslane Plants 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 causes of nosocomial infections and multi drug 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. On the other hand, medical properties of the extracts and essential oils against microbial as well as non microbial diseases have been known since ancient times and many studies have been performed on medical properties of the different plant species and their essential oil or extracts effects on microorganisms.

Methods: In this study, aqueous and ethanolic extracts were prepared from dried leaves of the Stachys schtschegleevi and Portulaca oleracea, then anti-bacterial activities of the extracts for Staphylococcus aureus were experimented, first by the method of well diffusion in agar, and later the amount of the MIC and MBC of the extracts 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 extracts) of extracts, to female BALB/c mice was intrapertioneally injected. Then, the counting of bacterial clonies 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 ethanolic extract of Stachys schtschegleevi (20 mm), and the minimum of growth inhibition diameter is related to ethanolic extract of Portulaca oleracea (10 mm) at the highest concentration (400 mg/ml). The results of broth microdilution method on Staphylococcus aureus showed that the amount of MIC and MBC in ethanolic extract for Stachys schtschegleevi were 52.5 mg/ml and 125 mg/ml respectively, while this amounts for ethanolic and aqueous extracts of Purtulaca oleracea and Stachys schtschegleevi were the same and equal to 125 mg/ml and 250 mg/ml. The aqueous extract of the Portulaca oleracea did not show any antimicrobial activity. In conditions of in vivo, after 48 hours spleen supernatant cultivation, the average number of bacteria for ethanolic extracts of the Stachys schtschegleevi and Portulaca oleracea were 1.8×103 CFU/ml and 6.6×103 CFU/ml respectively and for aqueous extract of Stachys schtschegleevi was 14.6×103 CFU/ml. 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 ethanolic and aqueous extracts of Stachys schtschegleevi and ethanolic extract of Portulaca oleracea have the effective antibacterial activity against mentioned bacteria and can be useful to treatment of nosocomial infections.

Keywords: Antimicrobial, Portulaca oleracea, Stachys schtschegleevi, Staphylococcus aureus

Antidermatophyte effect of zinc nanoparticle on Trichophyton mentagrophytes (Research Paper)

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Introduction: Recently Drug resistance is one of the main problems and researchers around the world are looking for the agreeable solution. Antifungal drugs are not far from this rule. With the expansion of nanotechnology, the use of nanoparticles in the treatment of diseases is one of the solutions. In this study, we used zinc nanoparticles. Zinc nanoparticles are one of the most widely used mineral nanoparticles that are considered by researchers due to their suitable physical and chemical properties. Zinc nanoparticles are used in the cosmetics industry, especially sunscreens and the food industry. Their antimicrobial properties have also been proven. One of the most common fungal diseases is Dermatophytosis That caused by Dermatophytes and affects on the skin, hair and nails. Trichophyton mentagrophytes is one of the most common dermatophytes. In this study, the effect of zinc nanoparticles on Trichophyton mentagrophytes was investigated.

Methods: T. mentagrophytes (PTCC5143) was prepared from fungal Collection of Tehran University and cultured in SCC and incubated in 28 ºC for 7-14 day. Zinc oxide nanoparticles was prepared from Nano Nasb Pars Company, the size of them was 20-50 nm. Antifungal effect of them was measured by disc diffusion method, Minimum Inhibitory Concentration (MIC80) by Macrodilution and Microdilution method, and Minimum Fungicidal Concentration (MFC).

Results: The results showed that the inhibition zone of the zinc nanoparticles were 24.43±0.5 mm which is not significantly different from that Griseofulvin ($p \leq 0.05$) and The concentration of MIC80 has been 6.25±0.5 mg/ml and the concentration of zinc nanoparticles obtained as an MFC has been 12.5±1 mg/ml which is not significantly different from that of Griseofulvin, Nystatin and Terbinafine ($p \leq 0.05$).

Conclusion: According to the results, the zinc nanoparticles had antifungal effect potential on Trichophyton mentagrophytes. As a result, the zinc nanoparticles are a very suitable and safe substitute for the treatment of fungal diseases such as dermatophytosis.

Keywords: Trichophyton mentagrophytes, zinc nanoparticles, dermatophyte

Antimicrobial effect of new compounds sulfadiazine-derived drug on Pseudomonas aeruginosa (Research Paper)

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Introduction: Pseudomonas aeruginosa is one of the most important causes of nosocomial infections that can cause widespread infections in patients with defective immune systems. Burn wounds are a good place for resistant infections and Pseudomonas aeruginosa is the most common bacteria that cause these infections. Therefore, research on obtaining effective drugs seems necessary. Sulfadiazine is a broad-spectrum sulfonamide antibiotic that inhibits bacterial growth and replication by inhibiting folic acid synthesis. This drug is used in combination with silver as a burn ointment. There are several studies on the use of this drug in combination with other drugs. The aim of this study was to evaluate the antibacterial effects of a new drug derived from sulfadiazine (sulfadiazine + 4-diamino benzaldehyde) on Pseudomonas aeruginosa.

Methods: For this purpose, 0.2 mmol of sulfadiazine with 0.2 mmol of 4-dimethylaminobenzaldehyde with 10 ml of acetic acid solvent at 110 ° C was refluxed on the heater for 10 hours at 200 rpm. The resulting orange precipitate was crystallized with 2-propanol to obtain a pure precipitate. Finally, the structure of the synthesized compound was confirmed by determining the melting point, C-NMR, H-NMR, TLC and IR. Then the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the synthesized drug on Pseudomonas aeruginosa were determined exerting microdilution method on Müller-Hinton broth medium.

Results: Different color, melting point and the results of C-NMR, H-NMR, TLC and IR indicate the new structure of the synthesized drug. The MIC and MBC of sulfadiazine-derived drug on Pseudomonas aeruginosa were 1 and 2%.

Conclusion: The synthesized drug effectively has antibacterial activity which can be used in pharmacy and treatment of infections caused by this bacterium.

Keywords: Sulfadiazine, Reflux method, Pseudomonas aeruginosa, Drug resistance, Antimicrobial effect

Antioxidant activity and cytotoxicity of tert-butyl p-nitroperbenzoate against MDA-MB-231 and MCF-7 human breast cancer cell lines (Research Paper)

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Introduction: Breast cancer is the second most common cancer worldwide among women. Chemotherapy is one of the prevalent treatments for breast cancer which is associated with various challenges including relapse, multidrug resistance, and undesired side effects. Hence, new anticancer agents should be considered. In this way, the cytotoxic activity of the synthesized tert-butyl p-nitroperbenzoate compound was evaluated against MDA-MB-231 and MCF-7 human breast cancer cell lines. In addition to the anti-cancer effect, the antioxidant properties of this compound were also investigated.

Methods: 2 mg of the compound was dissolved in 1 mL dimethyl sulfoxide (DMSO) to prepare 2mg/mL concentration and diluted in the culture medium. The final concentration of DMSO in the treated cells was 1%. To measure the cytotoxicity of the compound, the cells were seeded in a 96-well plate and incubated for 48 hours with different concentrations (8.36, 20.90, 41.80, and 83.60 µM) of the compound and doxorubicin as a positive control. The viability of the cells was measured by the standard protocol of the MTT assay. The half maximal inhibitory concentration (IC50) values were estimated by fitting the data in a sigmoidal dose-response curve based on non-linear regression analysis using Microsoft Excel for each cell line. Antioxidant activity of the compound was determined using DPPH and ABTS tests.

Results: Results showed that tert-butyl p-nitroperbenzoate has significant cytotoxicity activity with IC50 values of 42±0.02 and 107±0.04 µM on MDA-MB-231 and MCF-7 cancer cells, respectively. Also, tert-butyl p-nitroperbenzoate exhibited no DPPH and ABTS radical scavenging activities.

Conclusion: The results of this study show that tert-butyl p-nitroperbenzoate may be suitable for investigating the applicability of this compound for cancer therapy.

Keywords: Breast Cancer; Anticancer; tert-butyl p-nitroperbenzoate

Application of 〖Fe〗_3 O_4-Au hybrid nanoparticles for multimodal Computed tomography/magnetic resonance imaging and photothermal cancer therapy (Review)

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Introduction: Although cancer treatment has made great strides in the last two decades, their performance has not been satisfactory for reasons such as their ineffectiveness against metastatic diseases. Among the various types of cancer treatments, photothermal therapy (PTT) is widely used as a non-invasive method due to light-induced heating and ablation of cancer cells without damaging the surrounding normal tissues. In addition, the survival rate of cancerous patients depends on the stage of diseases. Recently, theranostics, have integrated diagnostic and therapeutic methods into a single platform to optimize cancer treatment. In this review, we investigated the application of iron oxide/gold(〖Fe〗_3 O_4-Au) hybrid nanoparticles(NPs) as dual-mode MR/CT imaging agents and simultaneously photothermal therapy of cancer cells.

Methods: The keywords of "〖Fe〗_3 O_4-Au nanoparticles", "CT", "photothermal therapy" and "MRI" were entered in the scientific databases of PubMed, Scopus, Science Direct and google scholar. 10 full relevant articles were extracted and reviewed.

Results: 〖Fe〗_3 O_4 NPs are used as a contrast agent in MR imaging due to the T2 shortening effect. Moreover Au NPs are coated on the surface of 〖Fe〗_3 O_4 NPs to improve chemical stability and biocompatibility. Studies have shown that gold nanoparticles are used as a suitable agent for CT imaging and PTT of tumors because of their high X-ray attenuation properties and near-infrared absorption (NIR) feature. The soft tissue contrast of CT imaging is lower than that of MR imaging while the spatial resolution of MR imaging is lower than that of CT imaging. Therefore, combining different diagnostic methods in single nanoparticle leads to an accurate diagnosis of the disease and eliminates the defects in one imaging modality. In studies the 〖Fe〗_3 O_4-Au NPs have shown a relatively high r2 relaxivity 136.4 mM/s (1.5T, 14nm), 245.12 mM/s (3T, 20nm) and also good X-ray attenuation property. In addition the 〖Fe〗_3 O_4-Au dendrimer stabilized nanoflowers displayed desirable photothermal conversion efficiency (82.7%) and excellent NIR absorption features.

Conclusion: From a review of studies, it can be concluded that iron oxide/gold hybrid nanoparticles can be used as suitable theranostic nanoprobe for multimodal

Computed tomography/magnetic resonance imaging contrast agent and photothermal therapy of tumors because of their unique features.

Keywords: 〖Fe〗_3 O_4/Au nanoparticles, MRI, CT, photothermal therapy and cancer

Application of bee venom to cancer (Review)

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Introduction: Bee venom (BV) (api-toxin) has been widely used in the treatment of some immune-related diseases and more recently in the treatment of tumors. Several cancer cells, including kidney, prostate, lung, bladder, and liver cancer as well as leukemia cells, can be targets of bee venom peptides such as melitin and phospholipase A2. The effects of cellular toxicity through the activation of prostaglandin PLA2 by melintin have been identified as an important mechanism for anti-cancer BV activity. Induction of apoptotic cell death by several mechanisms causes the death of cancer cells, which are activated by the activity of the caspase and matrix metalloproteinases, which are important for anti-cancer activity due to myelin. Combining cellular leptin peptide (melitin) with hormone and gene carriers of melitin carrier can be useful as a new treatment for some types of cancer, such as breast and prostate cancer.

Methods: Based on previous studies, in fact, melittin is known as a non-specific cytolytic peptide that can attack the lipid layer. Therefore, if injected intravenously, it can cause significant toxicity. Park et al., also reported that BV and its main component, melittin, inhibit the growth of cancer cells in the laboratory and inside the body by activating the pathways of caspases (3 and 9). It inhibits NF-κB signaling and its downstream reproductions, and produces anti-apoptotic gene products such as Bcl-2, cIAP-2, iNOS, COX-2, and cPLA2.

Results: However, many optimization methods have been used as malignant nanoparticles in pharmaceuticals. Significantly, raw BV, as well as the militancy of antitumor activity against a variety of cancer cells have been shown.

Conclusion: According to these studies, melittin inhibits HCC cells in vitro and in vivo with the help of Rac1. In addition, the combination of melatonin with a chemotherapeutic agent such as temozolomide significantly reduces growth along with melanoma cell invasion.

Keywords: Melitin. PLA2. Cancer. Bee venom

application of curcumin in the treatment of cancers (Review)

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Introduction: The use of traditional medicine in many nations comes from the culture and civilization of the people of that region. They used traditional medicine from far away times as medicine, but with the scientific advancement of peoples of different nations, they brought to the day of chemical medicine and moved away from traditional medicine. But with time and proof of the damage, many of these chemical agents of various nations turned into herbal remedies. Curcumin was isolated and identified for the first time in gross form in 1815 by Vogel and Peltier from the rhizome of the Curcuma longa plant, which was named curcumin. But they failed to identify the composition and chemical formula of this substance. In 2011, the structure and chemical formula of curcumin was identified by Milobedzka and his colleagues, and in 1913 Lampe and Milobedzka synthesized this compound. In 1953, curcumin components were measured and separated by Srinivasan chromatography. The chemical formula of curcumin is dione [3,5-heptadiene-6,1-(methoxyphenyl-3-hydroxyl-4) bis-7,1]. Its hydroxyl groups are essential for antioxidant activity and its methoxy groups for anti-inflammatory and anti-proliferation activities. Curcumin is soluble in water and ether, insoluble in ethanol and dimethyl sulfoxide (DMSO or Dimethyl sulfoxide) and acetone

Methods: Traditional medicine is a collection of knowledge, skills, and practices based on the definition of the health and medicine organization based on native theories and experiences, whether or not they can be used. Curcumin is a chemical substance that is the cause of the yellow color of saffron and turmeric. For many years, Chinese and Roman doctors have been using this plant to treat various diseases. According to studies, this chemical has various applications in the treatment of various diseases, including Types of cancers, alhob, arthritis, and so on. Accordingly, in this study, which was done by collecting data from various information desks, we studied the anticancer properties of this chemical and how it functions on different cancers.

Results: Curcumin is used to treat many cancers. If we look at it at the nanoscale, we will see more effective effects. Correquemin affects the molecular mechanisms of genes and, by their effect on their divisions, prevents their excessive proliferation.

Conclusion: Thus, according to studies, coccoquine, having an antioxidant effect with an effect on apoptosis, causes the death of cancer cells, or prevents the formation and growth of cancer cells by inhibiting the divisions of a particular gene and preventing the effect of that gene on the target cell. With more studies on this

substance, there is a hope that it will have a good place to treat cancers and treat many cancers.

Keywords: Curcumin, Cancer, Gene.

Application of e-Health in the mental health of healthcare workers during the Covid-19 pandemic (Review)

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Introduction: During COVID-19 pandemic healthcare workers (HCWs) are under significant mental health pressure. Studies indicated problems such as fear, anxiety, depression, sleep disorders among the HCWs, especially first-line staff are common. Many factors are involved in causing stress on HCWs in the current circumstances, including high workload, growing number of patients, high mortality rate of COVID-19 patients, lack of specific treatment and vaccines, lack of protective equipment, long work time, and insufficient support. Hence, interventions should be taken to reduce the negative effects of this disease on the mental health of HCWs. Adopting information technology could be effective way to manage this issue. Therefore, the present study aims to investigate applied technologies in the field of mental health of HCWs during the COVID-19 outbreak.

Methods: In order to identify applied technologies for managing the HCWs' mental health during the COVID-19 pandemic, a search was done in September 2020 through Google Scholar with the keywords of "SARS-CoV-2", "Healthcare worker", and "Information technology" alongside their synonyms. The studies which were related to monitoring or controlling of the mental health of HCWs through technological-based interventions during the COVD-19 outbreak were selected to extract information.

Results: According to the studies, several technologies were applied to manage HCWs' mental health. These technologies were applied to provide different services that could be categorized in three categories. The first category, called protective services, using technologies such as virtual clinics, robots, artificial intelligence, and mobile applications, were used to reduce the workload of HCWs, reduce provider-patient interactions, and ultimately prevent occurrence psychological problems in the HCWs. The second category includes supportive services in order to solve the psychological problems that the HCWs are engaged with them via providing the necessary training and counseling to them in the electronic context and through technologies such as video conference, telephone, and webinars. The third category includes diagnostic services and mental health monitoring of HCWs. Technologies such as sensors and wearable equipment, mobile applications, and online screening were used to monitor the mental health of HCWs during the COVID-19 outbreak. Therefore, in case of any disturbance, necessary warnings will be provided.

Conclusion: The COVID-19 pandemic caused several mental health problems among people especially HCWs who is under serious psychological pressure. Therefore, using information and communication technologies could be a beneficial approach. These tools provide services to manage and control the problems caused due to COVID-19 pandemic and represent useful statistics relating to mental health status of HCWs that could be bring attention of managers and policymakers.

Keywords: COVID-19, Pandemic, Mental health, Medical staff, e-Health

Application of Gelucire as Carrier for Solid Dispersion: a Literature Review (Review)

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Introduction: Gelucires are Polyethylene glycol glycerides which can be composed of PEG mono- or diesters and mono-, di-, or triglycerides. They are inert semi-solid amphiphilic excipients which can form a fine emulsion or solid dispersion upon contact with water. Gelucire different varieties are characterized by HLB values and melting point. Lipophilic drugs are insoluble or practically insoluble in water, hence their bioavailability must be considered as a usage limitation. Solid dispersion process with carriers which have high HLB values, has been known as a method for aqueous solubility improvement. As solid dispersion of lipophilic drugs with gelucires can potentially enhance their water solubility, the solid dispersion is investigated in many studies. In the current paper, application of gelucire as a solid dispersion carrier for lipophilic drugs is reviewed.

Methods: Internet based searches were performed June 2020 in PubMed and Scopus, using identified keywords. This search had considered papers which had been published in English and Persian, regardless of study design, for any condition and in any form.

Results: A total number of 31 studies were reviewed, in which solid dispersion of albendazole, allopurinol, α-tocopherol, artemisinin, bosentan, carvedilol, celecoxib, cinnarizine, diclofenac, etoricoxib, everolimus, flufenamic acid, flurbiprofen, indomethacin, lorataine, lornoxicam, meloxicam, naproxen, piroxicam, progesterone, saquinavir, spironolactone, temazepam, tiaprofenic acid, UC-781 and ursolic acid with gelucire 50/13 or gelucire 44/14, using various solid dispersion methods including solvent evaporation, co-grinding, co-precipitation, kneading, spray-drying and melting methods were studied. According to Fourier transform infrared spectrograms, depending to the drug, formation of a significant interaction between gelucire and the drugs might be possible. Quantitative evidence demonstrated that X-Ray diffractograms of the solid dispersions were smoothened comparing with the pure drugs and peak of drug melting point was not observed in differential scanning calorimetry thermograms which means that the solid dispersion process with gelucire decreased drugs crystallinity and improved their wettability. Solubility of the drugs was increased in both acidic (pH 1.0-1.2) and neutral (pH 6.8-7.4) after solid dispersion with gelucire. Moreover, dissolution studies indicated that the produced solid dispersions can be dissolved faster than the pure drugs in both simulated intestinal fluid and simulated gastric fluid. Furthermore, in vivo studies revealed that solid dispersion with gelucire was potentially useful for improving bioavailability of drugs.

Conclusion: On the basis of the study results, it can be concluded that utilizing gelucire as solid dispersion carrier, can be considered as an efficient method for bioavailability improvement of the water insoluble or poorly water soluble drugs. Further researches are suggested to be studied on gelucire potential application as solid dispersion carrier and the solid dispersion

Keywords: Gelucire; Solid Dispersion; Carrier; Bioavailability

Ascorbic acid (vitamin C) exhibit different effect on liver fibrosis in male and female mouse. (Research Paper)

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Introduction: Liver is the largest gland and one of the most important and sensitive organ in body. Liver fibrosis is one of the highly conserved response to liver injury that is observed in patients with chronic viral hepatitis, nonalcoholic fatty liver disease, alcoholic liver disease, cholestatic, and autoimmune liver disaese. The studies illustrate that progression of liver fibrosis leads to cirrhosis of the liver and hepatocellular carcinogenesis in the late stages. The role of various factors in reducing or increasing the incidence of hepatic fibrosis has been reported. Ascorbic acid is considered as a biosynthetic family co-factors and gene regulation of monoxygenase and dioxygenase enzymes that play a role in the synthesis of collagen.

Methods: In this study, the role of ascorbic acid in liver fibrosis induced by intraperitoneal injection of carbon tetrachloride in C57BL/6 adult mice will be examined. In fact, Mice were treated with ascorbic acid solution at concentrations of 1,2 and 3 g / kg for 2 weeks and one day in between. All mice were killed after 4 weeks and their liver was isolated and examined. the activities were achieved like measurement of liver weight (using balance), the incidence of fibrosis (using Masson Trichrome and Hematoxylin and Eosin staining), changes in blood serum enzymes including ALT and AST (using specific kits).

Results: The results of the study showed that ascorbic acid causes to change of liver morphological structures, increase in levels of ALT and AST in blood of the groups of males and females that get average dose of Ascorbic acid and rise the amount of liver injuries. While, these enzymes concentration in females that get low and high dose of Ascorbic acid decreases liver injuries.

Conclusion: generally, this study showed that ascorbic acid in some groups dependent on genus and dose increases the amount of fibrosis in CCL4-induced liver fibrosis. Therefore, as a therapeutic approach, the levels of ascorbic acid (vitamin C) in the blood of people with liver fibrosis should be investigate and control.

Keywords: fibrosis, liver,carbon tetrachloride, ascorbic acid, epigenetic

Assessing rs4994 polymorphism in the ADRB3 gene and its association with changes in the level of some biochemical factors in the body. (Research Paper)

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Introduction: According to WHO reports, Weight Gain is becoming the most serious public health problem and one of the most common causes of deaths in the 21st century, in children and adults worldwide. Weight Gain can have Genetics factors in addition to the acquired causes. Rs4994 polymorphism in ADRβ3 gene is one of the factors increasing body mass index in humans. During this single nucleotide mutation, the G mutant allele replaces A and converts the tryptophan amino acid to arginine. We scanned for the polymorphism of rs4994 (Trp64Arg) in ADRβ3 genes in Iran Tehran population to examine the relationship between this polymorphism and related disorders such as cholesterol levels, LDL, HDL levels and triglycerides.

Methods: We selected 201 adults from the population of men and women in Tehran Iran who were between 18 and 70 years old. Body mass index (BMI) waist/hip ratio were calculated. HDL, LDL, cholesterol and triglyceride concentrations were determined. ADRβ3 polymorphisms (rs4994) were screened by DNA sequencing. According to the World Health Organization, individuals were divided into three categories in terms of body mass index normal weight (BMI < 25 kg/m2), overweight (BMI ≥25.1–29.9 kg/m2) subjects, and obese (≥30 kg/m2).

Results: In people with high body mass index, all biochemical parameters other than HDL increased significantly compared to the control group. Also, people with a BMI of more than 25 kg / m2 had a higher waist circumference than people with normal BMI.

Conclusion: The findings of this study show that BMI (body mass index) was directly associated with increased Waist/hip ratio cholesterol, triglyceride and LDL levels.

Keywords: rs4994, ADRB3, BMI

Assessing the ability of newly synthesized compounds to detect amyloid fibril formation (Research Paper)

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Introduction: Neurodegenerative diseases are characterized by the presence of amyloid deposition. Many probes have been choice to attempt the detection of the amyloid deposits, but most of them are unable to cross blood-brain barrier, due to its low lipophilicity or present the permanent charge in their structures. Therefore, there is strong motivation to develop suitable compounds for in vitro fibril quantitation as well as for in vivo amyloid imaging.

Methods: In this study, we synthesized some novel barbituric and benzothiazole compounds and examine their potential property to quantitatively detect the amyloid fibrils of some non-disease related amyloidogenic proteins in comparison with native soluble proteins or amorphous aggregation.

Results: Our results showed that some of the synthesized compounds could selectively and specifically bind to amyloid fibrils while other compounds demonstrated a low-affinity binding. Furthermore, our synthesized compounds due to neutral charge and high lipophilicity essence might cross the BBB and detect the amyloid fibril in vivo.

Conclusion: These synthesized compounds based on selectivity and specificity parameters showed high binding affinity to amyloid fibrils in dye-binding studies. Uncharged barbituric/ thiobarbituric acid derivatives are supposed to cross the BBB. Hence, such dyes with better lipophilicity and without permanent positive charge can be a suitable candidate as a probe for early diagnosis to detect the amyloid plaque in neurodegenerative disease.

Keywords: Amyloid determination, Amyloid fibril, Neurodegenerative disease

Assessment of different doses of Nickel on BUN, Creatinine and Uric acid values in female Wistar rats (Research Paper)

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Introduction: Nickel is known as heavy metal spreading widely over environment. Also, Nickel is presented in many industrial and commercial uses. Although inhalation is considered as one of the main routes of this pollutant transmission, humans in general are exposed to Nickel by contaminated food and water sources. Nevertheless, due to limited absorption of Nickel through gastrointestinal tract, it has less importance compared to other routes. Toxic and carcinogenic effects of Nickel on humans and animals have been investigated via various studies during recent decades.

Methods: 32 female rats were divided equally into 4 groups. The first group considered as control, only received water by intraperitoneal injection and the rest obtained Nickel by doses of 10, 15 and 25 mg⁄kg intraperitoneally. Examination period takes 20 days and on days 8, 12 and 16 rats were injected. On 20th day, blood samples were taken from any rats for evaluating biochemical values and eventually under general anesthesia with Ketamine and Xylazine, rats were euthanized.

Results: Dose-dependent increases occurred in values of BUN, Creatinine and Uric acid. According to the levels of BUN, Creatinine and Uric acid of the 4th group, which are the highest among all the groups, the dose 25 mg⁄kg indicated as the most toxic dose in this investigation.

Conclusion: This study demonstrated that Nickel causes adverse impacts on rats. To sum up, it has been determined that renal toxicity is one of the principal destructive effects of Nickel on bodies.

Keywords: Nickel, Wistar rat, BUN, Creatinine, Uric acid

Assessment of Encapsulated Eugenol by Chitosan Nanoparticles on RA model (Research Paper)

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Introduction: Chitosan nanoparticles Eugenol describes as an effective antioxidant that can treat rheumatoid arthritis (RA) with the first remedial chemicals rather than Methotrexate. This research aimed to examine the impact of Chitosan Nanoparticles Eugenol on the healing process of experimental neonatal RA as opposed to Methotrexate as a potent Nano herbal agent.

Methods: In both genders, the neonatal Wistar rats induced rheumatoid arthritis divided into sham, control, treatment receiving Methotrexate, and the second treatment receiving encapsulated Eugenol by Chitosan Nanoparticles. Malondialdehyde, subsequently evaluated for lipid peroxidation as an oxidative stress biomarker by assay kit. Additionally, the expression of FOXO3 protein as an antioxidant and the expression of the TGF-β and CCL2 / MCP-1 genes, respectively, were assessed by western blotting and real-time PCR, and beside accompanied by a study of cartilage histopathology.

Results: Based on results, a significant decrease of Methotrexate and Eugenol encapsulated by Chitosan Nanoparticles observed in the serum level of MDA and FOXO3 protein expression compared to the control group. Besides, the herbal agent Nanoparticle and Methotrexate had a decreasing impact on the expression of TGF-β and MCP-1 genes, and a significant correlation between MCP-1 and TGF-β was observed.

Conclusion: In Collagen Induced Arthritis rats, inflammation, synovial hyperplasia, and development of the pannus were severe. This concluded that possibly Eugenol Encapsulated by Chitosan Nanoparticles and Methotrexate, due to immunomodulatory, anti-inflammatory, and antioxidant potentials, has a protective effect against RA. Nano Eugenol can be proposed as being capable of providing promising lines for treating autoimmune disorders such as RA.

Keywords: Chitosan Nanoparticles, Eugenol, MCP-1, MDA, Methotrexate

Assessment of Gender Differences in Temporal Bone Anatomy Using Computerized Tomography Scan Images in Iranian People (Research Paper)

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Introduction: The skull is one of the most important parts of the body used to determine gender in forensic medicine. Previous studies have focused on cadavers' skulls in races other than Aryan race. However, the aim of this study was to focus only on temporal bone of living people in our country and evaluate the metric differences between the two sexes.

Methods: In this is a cross-sectional descriptive analytical study, CT images of patients in Amir Aalam Hospital were selected by the quota-convenience sampling method during 2015-2017. Temporal bone metric indices were calculated and compared in two groups of men and women.

Results: The results showed a significant difference in lateral angle of internal acoustic canal, length of mastoid process and the length to width ratio of mastoid process between women and men. But the width of mastoid process, bone thickness and Hounsfield units of squamous part of temporal bone and the angle between squamous part and zygomatic process of temporal bone showed no significant difference between the two groups (men and women).

Conclusion: The findings of this study show that certain characteristics of temporal bone alongside other clues can be useful in sex determination. Furthermore, it has emphasized the importance of sexual dimorphism in human anatomy.

Keywords: Gender, Skull, CT scan, Temporal bone

Association between overexpression of CDK9 and the expression of DNMTs gene in mouse myoblast C2C12 cells during differentiation. (Research Paper)

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Introduction: Cdk9 is a member of cyclin-dependent kinases (cdks) that has been associated with cardiac differentiation. Increasing of Cdk9 expression level could moderate the epigenome. Also, DNA methyltransferases (DNMTs), responsible for the transfer of a methyl group from the universal methyl donor, S-adenosyl-L-methionine (SAM), to the 5-position of cytosine residues in DNA, are essential for mammalian development. There are four members of the DNMT family, including DNMT1, DNMT3A, DNMT3B, and DNMT3L. We proposed whether Cdk9 overexpression might affect the global genomic DNA methylation status by influencing DNMTs gene expression in mouse myoblast C2C12 cells during differentiation.

Methods: For overexpression of CDK9, the PCEP4/CDK9 plasmid was transfected to C2C12 cells. Transfected and control C2C12 cells were differentiated and the expression of DNA methyltransferase enzymes (DNMT1, 3A, and 3B) level was evaluated in transfected and control C2C12 cells by quantitative RT-PCR upon Cdk9 overexpression.

Results: Our results showed that Cdk9 overexpression outcomes in DNA methylation changes in mouse myoblast C2C12 cells. We indicated that, upon Cdk9 overexpression, the average expression levels of DNMTs in proportion to global DNA methylation were meaningfully increased in Cdk9 transfected cells. Our study showed that Cdk9 caused to promoted epigenetic changes and moderate global DNA methylation profiling of the myoblast cells during differentiation.

Conclusion: In this study, we showed that although the expression of CDK9 enhances the cardiac differentiation in early stage of differentiation, however the overexpression of CDK9 cause to increase expression of DNA methyltransferase enzymes level during the cardiac differentiation. This change inhibits the differentiation by DNA methylation of myomiRs and genes promoters.

Keywords: DNA methyl-transferases, CDK9, C2C12 differentiation.

Association of SARS- COV-2 Infection with Lung Microbial Community (Review)

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Introduction: Coronavirus disease 2019 (COVID-19) is a contagious disease, caused by SARS-CoV-2 virus. SARS-CoV-2 virus occupies the lung and leads to COVID-19 disease, which has been suggested to be affected by the lung microbiome. The biopsies of lung from dead patients infected by COVID-19 show that the mortality of COVID-19 are correlated with bacterial and fungal contamination. The most bacterial genera were Acinetobacter, Chryseobacterium, Burkholderia, Brevundimonas, Sphingobium, and Enterobacteriaceae, whereas the most common fungal genera was Cutaneotrichosporon. Moreover, the microbiome of the gut is changed in COVID-19 patients, influencing both the immunity and severity of the disease.

Methods: Many studies show a potential role for the interaction of the microbiota (both gut and lung) and host in regulating the pathogenesis of several important lung diseases. Acute respiratory distress syndrome (ARDS) is one of the general and extreme symptoms of COVID-19, where the gut- associated bacteria is enriched in the lung microbiome. Consequently, the bacterial displacement is facilitated by the highly penetrable capillary of alveolus, through the highly penetrable colon wall to the lung. Thus the lung becomes susceptible to opportunistic bacterial infections, leading to inflammation, infection and acute pulmonary damage. Furthermore, pneumonia is accompanied with microbiome alteration, where the microbial density increases and its diversity decreases. Bacteria, virus, fungi or protozoans are associated with pneumonia. Microbial dysbiosis has been shown in both COVID-19 and community-acquired pneumonia, due to the existing pathogenic and commensal bacteria. The pulmonary disease is also actuated by microbial dysbiosis of the lung and it might be foregoing by intestinal dysbiosis. The growth of some bacteria is particularly increasing in SARS-CoV-2 infection, leading to secondary pneumonia. Therefore Lung Microbial Community is a serious factor in making antiviral response and influencing the consequence of COVID-19 ARDS.

Results: Bacteriotherapy and using of probiotics could represent a complementary resource for the prevention and restoration of SARS-CoV-2 intestinal mucosa damage through the modulation of gut- lung axis microbiota and decreasing related inflammation. For example, after a respiratory infection, the lactic acid producing bacteria play part in enhancing the antiviral immune response along with increasing natural killer cell activity, whereas the production of pro-inflammatory cytokines are reduced. An effective interaction in constructing an immune response in the lung is also observed between COVID-19 disease and probiotics, particularly Bifdobacteria and Lactobacilli, namely L. gasseri. Veillonella spp. and Prevotella spp. . In addition, the attendance of pathogenic bacteria and probiotics could increase the

coronaviruses angiotensin 2 receptor (ACE2). Alteration of microbiota plays a role in down- regulation of intestinal ACE, which can lead to intestinal susceptibility and inflammation. Interestingly, lung microbiome pathways are notable in COVID-19 patients, as their changes are observed to be correlated with enhancements in energy metabolism, metabolism of cofactors and vitamins, purine- related to one-carbon metabolism, nucleotide metabolism, and drug metabolism and also with reduction in amino acid and carbohydrate metabolism. Recently, the Broncho-alveolar lavage fluid sample of COVID-19 patients indicated significant alteration in eighteen metabolic pathways.

Conclusion: Therefore, further analysis is valuable to find therapeutic solutions based on the impact of the lung microbiome on the process of COVID-19 disease. Also, we suggest investigation of major microbiota associated with the previously mentioned metabolic pathways, in order to find effective probiotics for reducing susceptibility to COVID-19 or disease severity.

Keywords: Microbial community (microbiota); COVID-19; Respiratory infection; Lung

Association study of rs11038167, rs11038172 and rs835784 of the TSPAN18 gene in Iranian schizophrenia patients (Research Paper)

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Introduction: Schizophrenia is a chronic mental disorder that affects about one percent of the world's population. The disease is mainly characterized by delusions, hallucinations, and cognitive deficits. While hundreds of family-based and twin-based studies have confirmed the high heritability of this disorder, yet the precise molecular mechanisms regulating the pathways triggering SCZ and the cause of the disorder remains unknown. Large-scale genome-wide association studies (GWAS) have introduced putative chromosome loci suggesting potential variants of small effect which cumulatively may provide helpful clues about the etiology of SCZ. In a recent GWA study, we aimed to offer a conclusive association between the risk of schizophrenia and three single nucleotide polymorphisms (SNPs) in the Iranian population. These SNPs are located within the intronic region of the TSPAN18 gene, rs11038167, rs11038172 and rs835784. However, the results across the following replication studies are inconsistent.

Methods: This study was performed on a total of 997 individuals comprising 496 SCZ patients and 501 healthy controls, all of the Iranian descent. The two groups had no significant differences in distributions of age and gender ($p > .05$). Genomic DNA was extracted from the peripheral blood of 496 SZ patients and 501 healthy controls. Genomic DNA was extracted via the salting-out technique from the peripheral blood of all subjects. Rs11038167, rs11038172, and rs835784 were genotyped using the PCR-RFLP method in all subjects. Association of the genotyped SNPs and SZ were tested using the chi-squared test and logistic regression models. Pearson's chi-squared tests were applied to test for significance in differences between genotype and allele frequencies between the two groups and also to assess any deviation from the Hardy–Weinberg equilibrium. The difference between genotypes in the two cases and control groups was further assessed under log additive, recessive, and dominant genetic models using SNPassoc package of R software.

Results: The mean age of the SCZ patients and control subjects was 43.34 ± 7.21 and 44.11 ± 8.84 years, respectively. The age of onset of the disease among patients was 33 ± 1.6 years with almost 8 ± 0.03 years of illness. Patients were comprised of 350 males and 146 females and the control subjects included 343 males and 158 females. We have found significant differences in allele frequencies of the rs11038167 and rs835784 polymorphisms and also in genotype distributions of all three SNPs. The A allele of the rs11038167 and rs835784 in addition to the AA genotype of the three polymorphisms was associated with increased susceptibility to schizophrenia.

Conclusion: These results confirm the significant association between rs11038167 and rs835784 and rs11038172 polymorphisms and increased risk of schizophrenia in the Iranian population suggested earlier in previous studies on the Han Chinese population. Further replication studies designed on a larger scale on the same and other populations are required to confirm the present findings. Functional explorations are desired to focus on measuring the degree of expression and precise localization of TSPAN18 in various brain regions. Also, the analysis of the dynamics of the protein product and its potential partners, as well as the profound understanding of how downstream possible enzymatic signaling transduction is regulated by TSPAN18 is required.

Keywords: Single nucleotide polymorphism; Schizophrenia; TSPAN18; Association

Associations between immune responses and the development of food allergy in infants (Review)

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Introduction: Food allergy (FA) is an unwanted reaction due to a specific immune response to exposure to a food that occurs frequently[1]. FA poses considerable clinical and public health responsibility affecting 2–10% of infants [2]. Cow's milk allergy (CMA), mostly is the first appearance of allergic pathology in early infancy [3]. Regulatory T cells (Treg) are an important cellular source in the context of FA and play a crucial role in this process [4-6].

Methods: The data were collected by searching PubMed, ScienceDirect, Google Scholar, Scopus, Cochrane database systematic reviews, and Islamic World Science Citation Center (ISC). By searching this database, 77 articles were found, 11 of them by reading abstracts were removed and 12 of them were included in this abstract. All articles chosen from English articles.

Results: The mother's leukocytes and Th2 cells could stimulate eosinophil recruitment. Some cytotoxic mediators which are released by the breast milk eosinophils can easily increase the permeability of the gut mucosa of the suckling infant and thus increase the passing of food allergens [7]. The statistical analysis of Perezabad et al. revealed that decreased Treg numbers were good predictors to recognize between controls and Cow's milk protein allergy infants [8]. In a study, it was reported that in the breast milk of mothers with a CMA infant, both cytokine and cellular composition are significantly different from those of mothers with healthy infants, and this might affect the health status of the breast-fed infant [7, 9, 10]. Vassella et al. has been reported that an increase in the number of eosinophils follows human breast milk contains be associated with maternal allergy [11]. Also, Th2 cells could be transferred to the infant, then can migrate to peripheral tissues such as the skin or the lung [7]. Treg cells are an important cellular source in the context of FA [4, 5]. Chen et al. proposed that Single nucleotide polymorphisms of the interleukin-10 gene are related to allergic diseases, therefore, it might perform a serious role in the pathogenesis of FA [12].

Conclusion: In human milk, the major Immune components access to the infant's immune system may affect it. Treg is an important cellular source in the context of FA and plays a crucial role in this process. FA may be associated with a modified Treg response to an allergen.

Keywords: food allergy, infant, neonate, immune response

Associations between residential greenness and preterm birth (Review)

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Introduction: Introduction: Recently, environmental factors have been suggested as a determinant of social health. Recent studies have shown that access to green space can affect pregnancy outcomes. In the present review study, we conducted a systematic review of all relevant studies with the aim of investigating the relationship between green space and preterm delivery.

Methods: Method: In this study, a review was conducted to obtain relevant studies from the English databases Pubmed, Scopus, Web of science and Persian databases Iran Medex, SID and Magiran with the English and Persian keywords green space and preterm birth with all possible search combinations.

Results: Results: Out of 6964 articles, 5 cross-sectional articles with inclusion criteria were reviewed. In qualitative evaluation of articles with STROBE index, 4 studies were of high quality and 1 study wewr of medium quality. In general, in these studies, counting and tree canopy indices, environmental quality index (EQI), Census Area Unit (CAU) and Vegetation Continuous Fields (VCF) indices have been used to evaluated green space exposure. No association was found between green space and preterm birth in most studies, and the rest of the studies showed conflicting results on the protective effect of green space on preterm birth.

Conclusion: Conclusion: According to the study findings, there is no relationship between green space and preterm delivery. Due to the existence of studies with conflicting results, it is suggested that more studies be done in this area.

Keywords: Census Area Unit, preterm birth, greenness

Attitudes of patients and families about the transmission of bad news in oncology wards (Research Paper)

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Introduction: Introduction: Transmitting bad news is one of the most important challenges in cancer patients. This study was conducted to evaluate the attitudes of patients and families of patients who were hospitalized with a diagnosis of cancer.

Methods: Methods: In this descriptive cross-sectional study, 200 patients and families of cancer patients (70 patients, 80 adult families and 50 sick children) were admitted to the oncology wards of Bandar abbas Hospital were selected by available sampling method. The data collection tool was a questionnaire that was set in 6 dimensions of person, appropriate time and place to give bad news, amount of information given, acceptance of bad news, factors affecting how bad news was transmitted and demographic information. The questionnaire was completed by interview.

Results: Results: Based on the findings, there is a statistically significant difference between age and attitude in terms of receiving bad news in all 3 groups ($p = 0.035$). Bad news (difference between groups: 0.013) and lower attitude than the other two groups in the dimension of factors affecting bad news (difference between groups: 0.006). Female patients have a lower attitude towards bad news ($p = 0.036$). In the family of adult patients, people with higher education have a lower attitude towards the person giving bad news ($p = 0.008$). Also, people with higher incomes have a higher attitude towards giving bad news time ($p = 0.036$). Living in a private home caused a higher attitude towards the appropriate place ($p = 0.033$) and the amount of information to give bad news ($p = 0.043$) and also in the families of patients with acute illness a higher attitude towards the amount of information given about bad news ($p = 0.023$). Individuals working in the family group of young patients had a higher attitude towards accepting bad news ($p = 0.03$).

Conclusion: Conclusion: The results of this study show that there is no significant difference in the attitude of the patient and the family of the adult patient and the family of the young patient, but there is a difference in some aspects of the attitude and compared to some demographic variables. Socio-economic and demographic of people to be considered.

Keywords: Bad news, Patient and family attitude, Cancer, Communication skills.

Back to the nature: thymoquinone as an enemy against Covid-19 life cycle (Review)

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Introduction: Nature is a great source of medicinal drugs or their precursors. many approved drugs are based on natural products. most of the time, natural products able to cross the biological barriers and penetrate cells, which enables them to be ignition points for the leads in drug discovery with desirable pharmacokinetic properties. Thymoquinone is a bioactive compound isolated from Nigella sativa. according to numerous pharmacological studies, thymoquinone has been found to be a very promising natural product. the components of this plant are known for its intense immune-regulatory, anti-inflammatory, and antioxidant benefits in obstructive respiratory disorders. a molecular docking study also gave evidence that thymoquinone decelerates COVID-19 and might give the same or better results than the FDA approved drugs. The aim of this review was to investigate the possible immune-regulatory effects of thymoquinone on the COVID-19 pandemic.

Methods: COVID-19 is a member of Beta coronaviruses like the Severe Acute Respiratory Syndrome Human coronavirus (SARS HCoV) and the Middle-East Respiratory Syndrome Human coronavirus (MERS HCoV). in the absence of specific antiviral therapies or vaccines, medical care is complemented with different combinations of broad-spectrum antiviral agents, antibiotics, hydroxychloroquine, and convalescent plasma transfusion. Thymoquinone, the main constituent of Nigella sativa, has demonstrated anti-inflammatory, anti-oxidant, anti-tumoral, and antimicrobial activities. recently, molecular docking studies have shown that thymoquinone may inhibit SARS-CoV-2 and interfere with its binding to ACE2 receptors. this can avert virus entry and replication inside the host cell. Furthermore, SARS-CoV-2 spikes can bind to a cell surface heat shock protein (HSPA5), which is upregulated during viral infections. molecular dynamics simulations showed that thymoquinone can interfere with the attachment of SARS-CoV-2 to the HSPA5 substrate-binding domain b (SBDb) on the stressed cells, and consequently may reduce the risk of infection. interestingly, thymoquinone was found to be effective against the avian influenza virus (H9N2 AIV) and a murine cytomegalovirus infection model. Thymoquinone has been shown to downregulate inflammatory cytokines, reduce NO levels, and improve organ functions and survival of sepsis in an animal model.

Results: Thymoquinone as a compound has revealed a remarkable immunomodulatory activity at specific doses. This perhaps through a redox mechanism, which decreases the systemic oxidative stress and inflammatory response. interestingly, thymoquinone has also been found to have a protecting effect against lung fibrosis and collagen deposition by modulating the nuclear factor Kappa-B (NF-κB) and the antioxidant enzyme nuclear factor 2 heme oxygenase-1

(Nrf2/HO-1) signaling pathway. virus-induced phagocyte activation is correlated with oxidative stress, not just because ROS is produced, but also because activated phagocytes also produce inflammatory cytokines by the activation of NF-κB. Actually, many genes are regulated by NF-κB, including inflammatory cytokines, COX-2, and iNOS. thus, NF-κB inhibition can suppress inflammatory genes, impede the cytokine storm, and reduce immune cells infiltration and activation, and, therefore, protecting against tissue and organ damage.

Conclusion: No effective therapy is yet available for the new species of Coronavirus, SARS-Cov-2. Thymoquinone is a natural plant product with high safety and low toxicity such that people take it as a diet supplement, and growing evidence from preclinical studies demonstrates that it effectively inhibits viral infection, alleviates the severity of lung injury through offsetting the cytokine storm, inhibits subsequent fibrosis, and increases survival rates, therefore, the time is probably appropriate to move thymoquinone from experimentation on the bench to clinical testing for the Covid-19 pandemic.

Keywords: : Thymoquinone, immunomodulatory response, Covid-19

Benefits of cow's milk and a good solution for treating infants with CMA (Review)

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Introduction: Among infants, breast milk is the most important food source But in some cases, infants are have to use a milk other than breast milk. Since cow's milk is the most available milk substitute , so in many cases cow's milk replaces breast milk, but some infants are have Cow Milk Allergy (CMA), which can be caused by IgE and IgG4 allergy, or T lymphocytes is related to casein, lactoglobulin, immunoglobulin, and other substances in milk.

Methods: In this study, we looked at articles from 2013 to 2019 that were published on PubMed, Google scholar, Web of science using keywords like CMA and allergies to cow's milk, infant allergies, cow's milk and breast milk to find the article were used.

Results: According to the articles used in the present study, cow's milk has many advantages but also has some disadvantages because it causes allergies in most babies and it can be harmful to diseases such as EOE and it can cause anaphylaxis. One of the main solutions can be Oral immuno therapy (OIT) as an alternative to cow's milk, such as camel's milk, due to the different protein structure compared with cow's milk, the use of baked cow's milk or the use of hydrolyzed milk (Its proteins are completely or incompletely hydrolyzed) and probiotic milk (Lactobacillus rhamnosus GG) is accompanied by hydrolyzed casein (EHF + LGG). There are other solutions such as non-allergenic diets such as FFED diets, the growth of resistant bacteria to Cma in the intestines of infected children, and the mother's use of dietary supplements to increase breast milk salts as a good alternative to cow's milk such as supplements Calcium.

Conclusion: The best and safest way to treat this allergy is to use baked milk or other milk, such as camel's milk or hydrolyzed milk, because the solution is safer, but other ways, such as different diets, are not the good solution because we have prohibition to use of cow's milk and its products. In addition, as the infant gets older, this allergy will decrease, and at older ages, the components of cow's milk will be tolerable for different people.

Keywords: CMA, Allergies to cow's milk, Infants allergys, Cow's milk

Bioelectromagnetic nanotranostic compounds based on photothermal therapy and magnetic resonance imaging. (Review)

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Introduction: Common cancer treatment methods are chemotherapy and radiotherapy. However, these methods have significant side effects, so recently new treatments such as photothermal therapy have been considered clinically. Photothermal therapy has major advantages such as high efficiency and less damage to healthy tissues. This method uses electromagnetic light radiation (with wavelengths in the infrared region) besides nanoparticle absorbers with high efficiency of converting light into heat. Magnetic resonance imaging (MRI) is a non-invasive, non-ionizing modality in diagnostic imaging. MRI performance is significantly improved by contrast agents. The synthesis and application of tranostic compounds that have both the power to enhance the contrast in MRI and the ability to increase the conversion efficiency of light into heat is possible in the context of nanotechnology. These tranostic compounds, which have both diagnostic and therapeutic aspects at the same time, can be brought from potential to actual state, as another application of bioelectromagnetic in treatment of cancers, by using the electromagnetic waves of MRI.

Methods: In this study, we reviewed and searched for the keywords "bioelectromagnetic", "photothermal therapy", "MRI" and "nanotranostics" in the scientific databases of Science Direct, PubMed and Google Scholar. About 10 fully relevant articles were found and reviewed.

Results: In most studies, iron oxide was used as a nanoparticle to increase the efficiency of light to heat converting and improve MRI contrast. Along with iron oxide, two derivatives of graphite including graphene oxide and quantum dot graphene were used as coats to reduce toxicity, facilitate transfer, and increase the excitation of nanoparticles by infrared light of the electromagnetic spectrum.

Conclusion: The use of nanotranostic compounds can improves the utilization of electromagnetic waves in both photothermal therapy and MRI imaging and can lead to accurate diagnosis and efficient treatment for cancer cells.

Keywords: "Bioelectromagnetic", "Photothermal Therapy", "MRI" and "Nanotranostics"

Bioinformatics analysis of differential expression Long non-coding RNA HOTAIR and related high targeting score miRNAs as diagnostic biomarkers in Tamoxifen-resistant breast cancer cells (Research Paper)

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Introduction: Breast cancer is a disease in which cells in the breast grow out of control. Tamoxifen (Tam) is a central component of the treatment of estrogen receptor positive (ER+) breast cancer as a partial agonist of ER. It has been clinically used for the last 30 years to successfully treat ER+ breast cancer. The most challenging issue with Tam use is the development of resistance in an initially responsive breast tumor. A group of non-coding RNAs are involved in the resistance of breast cancer cells to Tam. However, only a few of these non-coding RNAs have been clinically suggested as biomarkers for Tam resistance. Therefore, the search for non-coding RNAs in the blood of people with breast cancer treated with Tam can be suggested as a prognostic biomarker for the management of Tam resistance so that these patients can use another drug for treatment.

Methods: We compared the transcriptomes of Tam-sensitive and Tam-resistant MCF-7 breast cancer cells for identification of genes involved in the development of Tam resistance by using bioinformatics analysis and RNA seq data from GEO: GSE111151 number (Hultsch S et al., 2018). Important miRNAs (with high targeting score) that associated with HOTAIR RNA were searched through miRDB, StareBase, DIANA and miRcode tools.

Results: We found up-regulated expression of long non-coding RNA HOTAIR and negative expression relationship between hsa-miR-326, hsa-miR-4677-3p, hsa-miR-330-5p and hsa-miR-1277-5p RNAs with HOTAIR RNA in Tam-resistant cells.

Conclusion: An increase in HOTAIR RNA expression levels and a decrease in mir-196a-5p and hsa-miR-326, hsa-miR-4677-3p, hsa-miR-330-5p and hsa-miR-1277-5p RNAs expression levels in the blood samples of people treated with Tam, can be find as diagnostic biomarkers that the drug used for these patients should be changed because the patient cancer cells is becoming more resistant. It is hoped that future studies report more diagnostic biomarkers in resistant breast cancer patients.

Keywords: Tamoxifen-resistant, Breast cancer, Non-coding RNAs, Diagnostic biomarkers, Bioinformatics analysis.

Bioinformatics analysis of hsa-mir-141-3p target genes in ovarian cancer process (Research Paper)

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Introduction: These days, ovarian cancer is one of the common cancers in the world. There are many factors contributing to the aggravation of this cancer. This disease is also consisting as an inherited disease, so genetic factors may be able to increase to risk of cancer progression. According to the researches, miRNAs (small non-coding RNAs) and SNPs (single nucleotide polymorphisms) might develop the chance of ovarian cancer. The aim of this study is to diagnose a biomarker for the early detection of this cancer. Based on bioinformatics analysis, hsa-mir-141-3p of chromosome 12, was Chosen for this study.

Methods: Bioinformatics analysis of this study have been done by using miRbase, miRTarbase, miRWalk, TargetScan, DIANA TOOLS, DAVID, miRdSNP, miRNASNP, miRSNPdb, GeneMANIA databases and Cytoscape 3.8.0 software to get required data about micoRNA basis, validated and predicted target genes, genes' expressions, signaling pathways, SNP and genes' interaction networks.

Results: Based on hsa-mir-141-3p target genes, it has been revealed that KRAS, FGFR1, GRB2, MAPK8, PDGFRA, PDGFRB and PRKCA are considered as the most frequent genes which has vital role in Ras, PI3K-AKT and MAPK signaling pathways, that all show the same pattern in the ovarian cancer. Moreover, occurrence of rs3720 in KPNA3, a target gene, might have impact on the ovarian cancer progression, which in order to discover the exact role of this SNP in ovarian cancer, the further analysis is needed.

Conclusion: According to the surveys GRB2 gene, which has been operated by RTK cell surface receptors, activates Ras gene. By activation of KRAS gene that changes PIP2 to PIP3 during activation of cascade of genes, MAPK1 gene starts its function to agitate other genes that result in cell proliferation, differentiation and angiogenesis indirectly. Under various circumstances, activation of MAPK8 was shown to trigger cell inflammation indirectly. Accordingly, all foresaid genes, targets of the microRNA, leading to cancer. Evidences suggest that all the mentioned events help cell differentiation and proliferation, that outcome in ovarian cancer excessing which cause the metastatic process of ovarian cancer indirectly. Thus, hsa-mir-141-3p acts as tumor suppressor by inhibiting cell proliferation and differentiation. These findings might provide a promising therapy -for clinical treatment of ovarian cancer.

Keywords: Ovarian cancer, Bioinformatics, miRNA, SNP, Signaling pathways

Bioinformatics evaluation of targetom has-mir7-1-3p signaling pathway and related function of PCNA, SNP (RS3626) in patients with gastric cancer (Research Paper)

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Introduction: gastric cancer remains a major public health issue as the fourth most common cancer and the second leading cause of cancer death worldwide Environmental factors as well as genetic factors play an important role in the development and progression of this disease. With the introduction of microRNA into the genetic domain, these powerful molecules are opening up their place in the genetic domain of disease. miRNAs are small, non-coding molecules involved in various cellular processes, such as cell differentiation and death. Using bioinformatics databases PCNA gene with SNP (rs626) is effective in cell cycle signaling pathways in gastric cancer.

Methods: different genetics and environment risk factors can cause this csncer . therefor for fainding more bioinformatic informathion we use miRsnp,NCBI, miRbase,miRWAIK2.0,DAVID database and KEGG pathway

Results: in this study , bioinformatics predicted that , this microRNA (has-mir7-1-3p) is expected to target the rs3626 in coding region of the PCNA

Conclusion: the expected expression of PCNA and the negative regulatory function of the microRNAs would be expected . hsa-miR-7-1-3p increase and then decrease the expression of its target gene . for this reason ,the hsa-miR-7-1-3p is predicted to have a higher binding capacity to the rs3626 mutant(C) allele than to the dominant (G) allele of this SNP and may therefore be a risky mutant allele and cause cancer

Keywords: Gastric cancer, Single nucleotide polymorphism, ra3626, hsa-miR-7-1-3p , PCNA

Biological and non biological vectors as vaccine delivery vehicles for cancer therapy (Review)

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Introduction: Cancer is one of the leading causes of death that can cause 100 different diseases in different parts of the body, accounting for an estimated 9.6 million deaths, or one in six deaths, in 2018. Between 2007 and 2020, the number of deaths is expected to go up 15.2% in men and 8.1% in women. Cancer begins when changes begin, including the uncontrolled growth of cells. These cells may form a mass called a tumor. Gene therapy has received a lot of attention in the past few decades as an effective treatment for various cancers. Gene therapy relies on the introduction of nucleic acids or their synthetic analogs or genome-modifying proteins into cells to regulate gene expression with minimal off-target effect. A nucleic acid delivery system capable of delivering exogenous genetic material into specific cells. The exogenous genetic material that is delivered into cells by vectors, can be effectively expressed, and the delivery vector itself has low toxicity and does not interfere with the expression of genetic material. Nucleic acid delivery vectors are classified as biological vectors(Efficient transfection and expression but Exiting safety hazard and lacking targeting) and non-biological vectors. Non-biological vectors These vector-like Cationic liposomes are used as DNA delivery agents in gene therapy. Vector molecules form electrostatic interactions with DNA, therewith protects DNA from nucleases and cellular defense mechanisms. however non-viral vectors are safe for gene targeting, its low efficiency compared to viral vectors limits its application in cancer therapy. Research advancements along the years made use of bacterial and viral vectors or the combination of these with synthetic carriers to overcome the drawbacks associated with the use of non-viral vectors alone. Biological vectors (Viral vectors) Viruses are naturally immunogenic and may even stimulate the immune system. Their genetic material can be designed to carry the material we want to express in host cells Bacterial vectors Decreased tumor growth with Streptococcus pyogenes infection has been observed in a cancer patient if bacteria are used. Some bacterial components, like exotoxins, have been reported to initiate antitumor activities by their direct action on tumor cells rather than their indirect effect.

Methods: In Cationic liposomes vectors at physiological pH, the head group of positively charged lipids interacts with the phosphate groups of negatively charged nucleic acids to form a sandwich structure, in which a plurality of liposome particles encloses nucleic acid molecules. Some positively charged complexes are endocytosed or fused with cell membranes by charge to-charge interactions. In endosomal environments, the neutral lipids in cationic liposomes undergo a conformational change that results in the release of complexes into the cytoplasm, thereby avoiding the destruction of nucleic acids by lysosomes. Nucleic acids released into the cytoplasm unlock binding to cationic liposomes at a certain time and enter the nucleus at the time of mitosis to express the genes they carry. Viruses have the ability to infect human cells so they can be used as an effective

means of transporting vaccines because they trigger host T cell responses and humoral responses. Oncolytic virus-infected cancer cell process and present viral antigen to their surface, which are recognized by CD4+ and CD8+ T cells, resulted in T cell-mediated cancer cell destruction.

Results: With advances in the human genome project and advances in virology and related sciences, new methods for making non-pathogenic vectors are being developed. The above examples illustrate the different types of vectors commonly used in gene therapy. Each of these biological and non-biological systems has advantages and disadvantages that researchers are trying to use to their advantage. Viral devices are widely used and have a high transmission and expression efficiency, as well as stimulating the immune system and the potential risk of mutations.

Conclusion: New and sophisticated strategies for combating cancer are constantly being presented for gene transfer, as there is no set method for all types of cancer. The development of vectors and effective strategies for transfecting foreign DNA into specific cells is the ultimate goal in gene therapy. The use of recombinant bacteria and viruses is promising, and many researchers are currently working to complete this approach. Virus vectors used as recombinant vaccines activate the immune response of the host tumor through specific T cell immune responses.

Keywords: viral vector, non viral vector, gene therapy, cancer

Biosynthesis of magnetic iron nanoparticles(MINPs) by Lactobacillus fermentum and anti microbial effect of MINPs (Research Paper)

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1.
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Introduction: In the last decade, Nanotechnology has made significant development, especially in the medical sciences and used of nanoparticles,researchers has been much attention to synthesis of a different kind of NPs. Among them, Magnetic Nanoparticles are interesting for researchers because they have great usage such as in data storage, catalysis, and bioapplications including magnetic bioseparation and detection of biological entities (cell, protein, nucleic acids, enzyme, bacterials, virus, etc.), clinic diagnosis and therapy such as MRI and MFH , effective drug delivery and biological labels. Several methods used to synthesized magnetic NPs, but biosynthesis is a new way that used plants, algae and microorganism.In this study we used Lactobacillus Fermentum to biosynthesis of magnetic iron nanoparticles

Methods: L.Fermentum)PTCC 1744(was obtained from microbial collection of (IROST).It was inoculated in MRS broth and incubated in 37c and 5% co2 for 72 h. then that were centrifuged at 5000 rpm and their supernatant were used for further experiments. Aqueous Fe2O3 solution (10−3 M) was prepared and added to supernatants of L.fermentum(10% v/v) in ambient condition.The production of iron nanoparticles was proved by changing the color of the solution, uv-vis spectroscopy ,XRD ,FTIR and TEM .Antimicrobial effect of them was measured by disc diffusion method.

Results: The color of solution was Indian red, change of color to dark brown showed that INPs were produced.The reduction of the Fe2+ ions by the supernatant of this bacteria and formation of INPs were monitored by UV_visible spectroscopy and they were showed a peak during 400-500 nm.According to the results of FTIR, the effective group in this reaction was the hydroxyl groups (pick in 3331.18 cm-1) and carbonyl groups (pick in 1659.00 cm-1). The formation of INPs was provided by X_ray diffraction (XRD) technique using an X_ray diffractometer with radiation λ = 54.1 Å for Fe3O4 and ƛ=33.2 for Fe2O3 over a wide range of Bragg angles.Based on the documents from the JCPDS data, the diffractions of 200, 311, 511, 440 in the angles 30.4, 35.8, 43.5, 54.1 , show the presence of Fe3O4 magnetic nanoparticles. The presence of a peak at an angle of 33.2 degrees indicates the production of Fe2O3. The shape of them was spherical and dimensions are 34-44 (nm) was expected. TEM results showed thatSize of the INPs formed by the supernatants of Lactobacillus fermentum was 20-30 ±1 nm and spherical shape. The results of the antimicrobial effect was,Inhibitory zone inEscherichia coli19± 0.4mm,Staphylococcus aureus16.5± 0.41mm,Bacillus subtilis39 ±1mm,Pseudomonas aeruginosa11 ±0.5mm ,This results showed that the INPs was effective.

Conclusion: According to results, we have successfully extra cellular synthesized of INPs by Lactobacillus fermentum supernatants. This method is simple, safe, cost effective and eco-friendly.INPs produced by this method are very small and also Lactobacilluses are the major group of probiotics, so this bacteria are safe and without pathogenic effects. So we can definitely used of them in medical and pharmacology purposed

Keywords: Magnetic Iron Nanoparticle , Probiotic , Lactobacillus fermentum ,Biosynthesis

Blocking Protein, Reelin: a novel treatment strategy for multiple sclerosis (Review)

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Introduction: Multiple sclerosis is a neurological autoimmune disorder, affecting approximately more than 2.3 million people throughout the world. in MS, circulating immune cells penetrate into the CNS (the brain and spinal cord), where they wrongly attack myelin, the protective sheath that covers nerve fibers, and elevate inflammatory reactions, subsequently cause nerve cells to die. various therapies for MS, approved or in development, attempt to prevent immune cells from infiltrating the CNS to cease neuroinflammation, demyelination (loss of myelin), and disease progression. however, serious side effects are known with most of these approved therapies, emphasizing a need for better and safer immunomodulatory approaches. Reelin is a key protein secreted from brain and some other organs and has function on brain development, neural connection during adulthood, and also act on endothelial cells (those lining blood cells), regulating the adhesion and passage of monocytes to and through the endothelium consequently regulates how permeable blood vessels are to immune cells. this suggests decreasing the amount of this protein significantly protected against development of the disease's characteristic symptoms and promoted recovery in multiple sclerosis. The findings could lead to a new treatment strategy for this neurological disease and other conditions marked by chronic inflammation. This study attempts to review related researches.

Methods: Multiple sclerosis(MS) is a demyelinating disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged. Interrupt in the ability of parts of the nervous system to transmit signals, resulting in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems. In the meantime, there is a great need for a treatment that covers a wide spectrum of MS. Reelin is a key. initially, it recognized only for its role in guiding neurons during brain development and as a synaptic homeostatic regulatory. Recently reported non-neuronal function for systemically circulating Reelin in the vasculature, where Reelin regulates the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)–mediated expression of several vascular adhesion molecules. findings revealed that circulating Reelin promoted the vascular inflammatory response by increasing leukocyte-endothelial cell adhesion and the increased expression of mRNAs encoding endothelial adhesion molecules. examining blood concentrations of Reelin in patients with relapsing-remitting MS (the most common form of the disease), scientists found that while Reelin concentrations were about the same in patients in remission as those without the disease, concentrations were elevated in patients during relapse. Investigating further, scientists worked with mice affected by a disease called experimental autoimmune encephalomyelitis (EAE), a condition that mimics human MS. these animals were genetically modified so that the researchers could control Reelin

production and some cases received antibodies against circulating Reelin using immunodepletion procedure.

Results: Findings reveal that eliminating Reelin substantially mitigated the disease's typical paralysis or even eliminated it altogether, in contrast to mice with normal Reelin levels. These effects appeared to originate the lack of monocyte adhesion on the altered animals' blood vessel walls, which inhibit entry into the central nervous system. Reelin appears to regulate the production of adhesion molecules on blood vessel walls that capture circulating monocytes. When the scientists decreased Reelin in animal models, levels of these adhesion molecules also declined, preventing them from capturing monocytes and causing inflammation. This strategy was even effective in animals that already displayed symptoms of the disease -- a situation that more closely mimics human patients diagnosed with MS -- reducing paralysis severity and promoting healing.

Conclusion: MS, a disease for which several effective drugs exist that nevertheless can have significant side effects .these findings suggest that circulating Reelin levels might correlate with MS severity and stages, and that lowering levels of Reelin may be a novel way to treat MS. some suggest that reducing immune cells' ability to accumulate and cause inflammation by altering Reelin levels could represent a new strategy for treating patients with MS. wondering if Reelin plays a similar role in other inflammatory diseases. MS, a disease for which several effective drugs exist that nevertheless can have significant side effects .these findings suggest that circulating Reelin levels might correlate with MS severity and stages, and that lowering levels of Reelin may be a novel way to treat MS. some suggest that reducing immune cells' ability to accumulate and cause inflammation by altering Reelin levels could represent a new strategy for treating patients with MS. wondering if Reelin plays a similar role in other inflammatory diseases.

Keywords: Multiple sclerosis, reelin, inflammation

Can triple-negative breast cancer be treated with PARP inhibitors? (Review)

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Introduction: Poly (ADP-Ribose) Polymerase 1 (PARP1) is an enzyme with a key role in the recovery of cells from DNA damage. There are pieces of evidence concerning the positive therapeutic efficiency of PARP1 inhibitor in breast cancer with or without mutation in BRCA. Therefore, evaluation of the PARP1 inhibitor as a new targeted therapy has been considered in triple-negative breast cancer (TNBC). TNBC is a heterogeneous subtype of breast cancer with aggressive clinical behavior and negative expression of ER, PR and Her2 results in a lack of targeted therapy.

Methods: Published scientific literature and clinical trials concerning the importance of PARP1 inhibitor in breast cancer with mutation in genes other than BRCA and sporadic TNBC were reviewed from 2000 to 2020. Searches were carried out using Goole scholar and Pub Med.

Results: According to the results, although PARP1 inhibitor therapy predominantly targeted breast cancer with a germline mutation in BRCA, it also can have positive therapeutic efficiency in breast cancer with somatic mutation in BRCA, the mutation in genes other than BRCA or exhibited BRCAness.

Conclusion: PARP1 inhibitor in cancers with beyond BRCA-mutant showed promising results to be considered as targeted therapy. These findings would provide a strategy for expanding the clinical trials on PARP1 inhibitor-based therapy in sporadic TNBC.

Keywords: triple-negative breast cancer; sporadic TNBC; targeted therapy; PARP1 inhibitor

Cancer,prevention,distinction and cure (Review)

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Introduction: uncontrolled cell proliferation that is normalized from growth and division.the exact cause of cancer is not known,for example,due to genetic and external factors that cause cell dysfunction.some researchers have found that a lack of protein called (GRB2) has the potential to control the growth and division of cells,which can lead to cancer. Tumors have2 categories.a group of inverters can be used to disable a part of the body by expanding it, and the other type cannot be moved,the first group of tumors is displayced by the circulatory system and lymph nodes.for example,following some tips like:no obesity,smoking,alcohol and avoidance of dangrouse parties and not being dexposed to some viral infenctions and knowing some genetics issues such as tumor gens.having high_risk sexual behaviors can be prevented.the risk increases with age.having healthy lifestyle,such as eatin healthy foods,is another point that keeps people about 30to50 percent away from this disease.treatment options include:chemotherapy,surgery,tissue therapy and even positive thinking and hypertension.some times treatments such as photodynamics are used to remove cancer cells and burn the tumor with a laser.symptoms of cancer vary depending on wich part of body the cancer is in and what the cancer is.some of the symptoms that a person notices include:injuries and bleeding,bloody coughs,bloody stools,hematuria,such as sudden and unwanted loss weight,fever,severe fatigue,skin changes.knowing the symptoms alone,it is not possible to tell if a person has cancer.by using common medical tests such as:blood tests,x_ray,ct scans and endoscopy can be detected.depending on where the tumor is located in the body, the type of treatment and the method of diagbosing the disease are also selected.

Methods: By review articles and books

Results: Cancer is a common disease that affects people around the world at different ages.parial cells of body divide at an uncontrollable rate and they go to other parts of the body and they sprease the disease such as blood,skin,digestive system,respiratori system,bones,etc.there is many treatments for them that depending on the type of tumor and the location of that.howevere,due to the interoduction of some points such as having a healthy life(kind of life style like:not smoking,healyhy food,not use alcohol and..)we can avoid the risk of cancer.

Conclusion: by identifying what cancer is,and gettind to know more people whith the disease and knoing how to prevent and treat the symptoms of the disease,we can help control and reduce the number of patients.

Keywords: cancer,cure,disease,prevention

CAR T cells : potential therapeutic option of multiple cancers (Review)

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Introduction: CAR T cell therapy, as a novel immunotherapy approach, has indicated successful results in the treatment of hematological malignancies; however, distinct results have been achieved regarding solid tumors. Tumor immunosuppressive microenvironment has been identified as the most important barrier in CAR T cell therapy of solid tumors. Developing novel strategies to augment the CAR T cell safety and efficacy could be useful to overcome the solid tumor hurdles. CAR T cell therapy, similar to other cancer treatments, can cause some side effects which can disturb the healthy tissues. In this review, we will discuss the effective breakthroughs in CAR T Cell therapeutic approaches by using the multi-targeted and programmable CAR T cells instead of conventional CAR T cells. These superior types of CAR T cells have been developed to increase the T cells' functionality and safety in a controllable manner. Also, by the use of multi-targeted and programmable CAR T cells, the incidence of side effects would be diminished. Moreover, we will describe the capability of these powerful CARs in targeting multiple tumor antigens, redirecting the CAR T cells into specific target cells, incrementing the safety of CARs, and other advantages that lead to promising outcomes in improving the CAR T cell therapy of cancers.

Methods: Searching online on google scholar, PubMed, and Scopus based on the keywords including Chimeric antigen receptor T cell, CAR T cells, cancer, and malignancy.

Results: Cancer is the most substantial death cause in the world, with several unknown complex mechanisms that usually lead to treatment failure. Based on immunotherapy, diverse treatment approaches have been developed to improve the success rate of cancer treatment in recent years. Adoptive cell therapy (ACT), as an immunotherapy strategy, has been developed to target the tumor cells by using the patient's immune cells after ex-vivo engineering and expansion . Interestingly, chimeric antigen receptor T cell therapy (CAR T cell), as an ACT therapy, emerged as a breakthrough in cancer remission during recent years. The chimeric antigen receptor is a recombinant receptor that is composed of the antigen-binding portion and T cell function portion. The antigen-binding domain usually is originated from tumor antigen-specific monoclonal antibody named ScFv. The functional domain consists of a signaling domain with or without the co-stimulatory domain. CAR T cells are clustered into four-generations based on having or not having the co-stimulatory domain. The CAR T cell proliferation, cytotoxicity, and persistence in tumor sites are improved in the 2nd, 3rd, and 4th generations. To date, Chimeric Antigen Receptor (CAR) T cell therapy has made revolutions in the treatment of refractory and/or relapsed (R/R) hematological malignancies. Targeting CD19 antigen on B cells has demonstrated long-lasting remissions in some B cell lymphoid malignancies such as non-Hodgkin Lymphoma (NHL) and Acute Lymphocytic Leukemia (ALL). Although encouraging results using CAR T cells have been indicated in hematological, limited efficacy has been

demonstrated in solid tumors. The most important limiting cause is the presence of an immunosuppressive microenvironment in solid tumors. Despite abundant obstacles in solid tumors, some improvement strategies have been developed to engineer powerful CAR T cells to overcome solid tumors. Given that the CAR T cell therapy, the same as other treatments, causes some side effects which may lead to healthy tissue damage, it is critical to enhancing their specificity and security. Since conventional CAR T cells are designed with fixed specificity to target a specific tumor antigen without any potential to regulate their function. On the basis of this, some adjusting mechanisms have been developed to control the CAR T cell performance and inactivate it after tumor cell elimination. The multi-targeted and programmable CAR T cells are the most momentous regulation strategies promoting the safety and specificity of the CAR T cells. Most of them can also target multiple tumor antigens accurately and simultaneously, which leads to tumor elimination more efficient than targeting a single antigen by classical CARs. In this study, we will discuss distinct types of multi-targeted and programmable CAR T cells and the plentiful advantages of using them investigated in several studies previously.

Conclusion: CAR T cell therapy has demonstrated promising results in hematological cancers. However, in solid tumors, the low success of CAR T cell therapy has been reported due to the existence of several barriers. To overcome the hurdles of CAR T cell therapy in solid tumors, new approaches have been developed to armor the CAR T cell. Genetically alteration of the CAR T cell or the utilization of the regulatory mechanisms is some examples (4, 9). Production of conventional CAR T cells requires autologous T cells to engineer, which takes a long time, high cost, specialist individuals, and intricate equipment. Also, the lack of regulation system in Conventional CARs can lead to a high incidence of side effects, which is caused by the uncontrolled overactivity of CAR T cells. Some regulatory methods have been developed to manage the CAR T cell function, such as genetically modification of CARs, designing inhibitory CARs, editing CAR T cells using CRISPR/Cas9 system, designing on-switch/off switch mechanisms, and suicide genes. These approaches have been applied to improve the performance and safety of CAR T cells. Multi-targeted and programmable CAR T cells include Dual CAR, Tandem CAR, SynNothch CAR, Universal CAR, and SUPRA CARs, are a new generation of CAR T cells with a flexible receptor that can target various tumor antigens concurrently with high efficacy and low toxicity. Moreover, other useful programmable CAR structures consist of Physiological CAR, split CAR, and TRUCK cells that can hopefully improve the CAR T cell therapeutic approaches. According to several previous studies, the activity of the mentioned CAR T cells is regulated through the split structure of the receptor or other manageable mechanism that decreases the common side effects of CAR T cells. Additionally, more effective cytotoxicity, high concentration of cytokines production, long persistence of T cells, overcoming the antigen tumor escape, enclosed anti-tumor responses to the tumor microenvironment, and low incidence rate of "on-target/off-tumor toxicity are the superior advantages of using Multi-targeted and programmable CAR T cells compared to conventional CARs. Despite the related advantages to mentioned smart CAR T Cells, various measures and investigations about their efficacy and safety should be performed. Most of the multi-targeted CARs have the capability of eliminating tumor cells, which only present two or

multiple antigens but no ones with expressing a single antigen. Therefore, it is better to say that some questions about the efficacy of multi-targeting CAR designing are unanswered. Additionally, target antigen loss is the only immune escape mechanism that multi-targeted CARs can solve it. Immunogenicity is another critical issue that should be considered due to the generation of unwanted autoimmune responses like human anti-mouse IgG antibodies (HAMAs), which can lead to anaphylaxis. To solving this problem, CAR T cells can be designed by the use of ScFv derived from humanized or human monoclonal antibodies. Further, using the autologous T cells instead of allogenic ones can improve the safety and efficacy of CAR T cells. CAR T cells proliferation and persistence are the other two crucial challenges required for the durable of CAR T cells in the tumor microenvironment during tumor eradication. For this reason, engineered CAR T Cells with long-live can increase the CAR T Cells' survival. In conclusion, the development of these dominant types of CAR T cells can significantly increase the CAR T cell efficacy and safety as a practical immunotherapy approach for various cancers treatment; however, our information about the in vivo function of these CARs and related side effects is limited. So, more studies in this field would be required.

Keywords: Chimeric antigen receptor T cell, CAR T cells, cancer, and malignancy.

CCAT2: A new molecular marker in the diagnosis and treatment of Breast tumors (Review)

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Introduction: Long non-coding RNAs (Lnc-RNA); are a heterogeneous group of RNAs with a length of 200 to 100,000 nucleotides Which are transcribed by eukaryotic RNA polymerases II & III at any point in the genome. These RNAs play an important role in detecting cellular processes that cause cancer phenotypes, such as proliferation, invasion, and survival. Changes in their expression, in addition to being a secondary sign of cancer, can also be directly involved in the onset and progression of cancer. LncRNA acts as a biomarker to monitor tumor prognosis as well as regulating gene expression to regulate the growth and progression of many cells, especially malignant tumors. Among the types of lnc-RNAs, we can mention the CCAT2 gene, which is found in high levels in cancer cells and tissues. Which is evaluated as an important molecular marker in the diagnosis and treatment of breast cancer. CCAT2 is probably a proliferative marker, meaning that whenever cell growth is high, the expression of this gene increases, and when its expression is inhibited, it reduces cell proliferation and differentiates progenitor and cancer cells. This gene is involved in the progression of the tumor from the lower stages to the higher stages of the malignant form, so it is possible that by inhibiting the expression of this gene through molecular methods such as RNAi, the progression of these tumors to higher stages of malignancy and metastasis can be prevented

Methods: In this review study, articles related to the CCAT2 molecular marker, using keywords CCAT2, lncRNA, Breast Cancer and long noncoding RNAs, from 2010 to 2020 in PubMed, Science Direct, Google Scholar, Springer Link and SID databases are searched and checked.

Results: Overexpression of CCAT2 significantly causes proliferation and attack of malignant tumors and is associated with tumor size, clinical stage, and TNM classification, indicating that CCAT2 is a significant biomarker for monitoring tumor progression. CCAT2 plays a key role in biological processes of tumor progression through various pathways. The results obtained from the review of articles in this field showed that the expression of CCAT2 gene in breast tumor samples increased significantly compared to marginal non-tumor samples. CCAT2 can be used as a new molecular marker to predict metastasis and prognosis in various human cancers, especially breast cancer.

Conclusion: According to our studies, the use of CCAT2 gene as a diagnostic marker in separating and identifying breast tumor tissues from non-tumor types is appropriate; Because CCAT2 gene expression also increases as the tumor progresses to higher stages. Therefore, by inhibiting the expression of this gene through molecular methods such as RNAi, the progression of these tumors to higher stages of malignancy and metastasis can be prevented. Therefore, the study of the expression of this gene can be used along with other conventional laboratory diagnostic methods.

Keywords: CCAT2, lncRNA, Breast Cancer, Long non-coding RNAs (Lnc-RNA)

challenges of creating cellular disease models using CRISPR (Review)

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Introduction: The use of CRISPR system has advantages in the field of disease modeling . The researchers used CRISPR to build models of human disease by knock-in , knock-out and indel mutations . So CRISPR/Cas9 can be used to create cancer-causing mutation in human cell lines and animal models . The CRISPR/Cas9 system has been recently used in disease-focused research to product and characterize patient-drived IPSCs with a specific genetic disease . The discover of human IPS cells in recent decades has opend a new window into disease modeling . The IPS cells have been generated as an in vitro disease model for disease such as Duchene disease and Down syndrome/trisomy 21 . These cell can be adapted to drug discovery with help of high throughout compound screening technology . The IPSCs cells have good advantage for pesonalized medicine because they can be derived from the patient themselves and thus do not stimulate the immune system when transplanted. But these model have some challenges.The purpose of this review article is to examine the challenges of creating cellular disease models using CRISPR.

Methods: In this review, pubmed, sciecedirect and wiley library sites were used. The keywords used to search these sites were crispr and disease model. After collecting the articles, the challenges in this field were studied.

Results: In disease modeling , it is possible that IPSCs derived from a disease caused by mutation. The main drawback here is that there is a difference in the genetic backgrounds of the control and disease groups ,a major problem in the study of human disease in the cell culture field is in long-term latent disease such as Alzheimer's , that it is be difficult to in vitro . Also IPS cell are limited in reusing complex tissue arthitecture in terms of cell complexity. This limitation has challenged the analysis of physiological and system-level phenotype .The one of IPS cells that use to cell disease creation are human ips cells (hIPSC) . These cells have some disadvantage . Limited sample size is one of the major disadvantages of these cells. In addition, to ensure the production of hIPSC cell lines, extensive validation is required, such as differentiation potential, lack of re-planning, and so on. The production and approval of hIPSC is time consuming and expensive. Another problem with hipsc studies is that an unexpected amount of variability may occur .

Conclusion: Genome manipulation in IPS cells or cultured in vivo has the potential to treat disease. Especially disease caused by single gene mutation. Patient drived IPS cells can be modified with CRISPR technology , selected in vitro and returned to the patient for replacement instead of disease cell .Although the latest genome editing tool has been used in the production of cellular and animal models, but the therapeutic ability of genome editing has still been delayed due to biological and ethical barriers. Another important issue is the ethical concern about the use of

CRISPR technology in humans. Advances in genome repair will allow us to learn more about the development and pathogenesis of the disease .

Keywords: CRISPR , IPS , disease , model

Changes in the ultrastructure of oocytes / follicles with polycystic ovarian syndrome following freezing-thawing (Research Paper)

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Introduction: Background and purpose: Polycystic ovary syndrome (PCOs) is one of the most common causes of infertility. In cases where fertility does not occur naturally, assisted reproductive techniques are used. One of the methods of assisted reproduction is the cryopreservation. The freezing of oocytes was done for a number of reasons such as; ovarian hyperstimulation syndrome, chemotherapy, parental conflict to have another child which will be felt more in the coming years. There are problems during oocyte freezing-thawing process, including damage to the mitotic spindle and the internal organelles of the oocyte, which is the purpose of the present study.

Methods: Materials and methods: 10 NMRI mice were divided into two groups: control and PCOs group. The PCOs mice were induced by intramuscular injection of 4 mg/kg estradiol valerate dissolved in 0.2 mg Sesame oil once a day. After 60 days, mice in each group were sacrificed, and ovarian tissue collected. The oocytes / follicles were freezed . Thawed oocytes and follicles were cultured for 24 hrs and then examined for ultrastructural changes by transition electron microscopy (TEM).

Results: Results: The freezing process causes vacuoles to form in the oocyte system, which may indicate structural damage. Occurrence of vacuoles in immature oocytes eventually leads to reduced ovarian competence for fertilization or evolutionary disruption in the early stages of the fetus. Ultrastructural changes in mitochondrial complexes and smooth endoplasmic reticulum vesicles were observed in the GV group, which could potentially justify the reduction of ejaculatory efficacy for fertilization due to impaired calcium homeostasis. The size of mitochondrial accumulations and smooth endoplasmic reticulum in the freezing group is smaller than the control group. The follicles are relatively healthy with a clear membrane.

Conclusion: Conclusion: Freezing and thawing process of PCOs oocytes/follicles lead to damages in internal organelles.

Keywords: Keywords: Polycystic ovarian syndrome, Vitrification, Thawing, Oocyte, TEM.

Chemical evaluation of active compounds, antioxidant and antimicrobial effects of Trachyspermum Copticum seeds harvested in Yazd province (Research Paper)

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Introduction: Trachyspermum copticum as a medicinal plant has many healing properties including: anti-flatulence, anti-vomiting, anti-rheumatic and expectorant. The aim of this study was to identify the active compounds, antioxidant and antimicrobial effects of Trachyspermum Copticum seeds harvested in Yazd province.

Methods: The essence of the seeds was first extracted by Clevenger apparatus. The active components of the essence were then separated and identified by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS) methods. The anti-oxidant effect was determined by DPPH (2, 2diphenyl-1-picrylhydrazyl) test as the half maximal inhibitory concentration (IC50) and the total amount of phenolic components of the essence was quantified utilizing the Follin-Ciocalteu method and measurement of MIC (minimum inhibitory concentration) of the product, anti-microbial activity.

Results: Our study shows that thymol (64.9%) and Terpinene (11.1%) were the most prevalent components of the essence. Also, the anti-oxidant activity and the total amount of phenolic component of the essence were 0.799µg/ml-1 and159.87 mg/g-1 resepectively and the standard AATCC microbial test showed inhibitory effect of bacteria, especially Pseudomonas aeruginosa and Streptococcus pneumoniae indicated acceptable properties.

Conclusion: The results of this study showed that the active ingredients of the native plant Trachyspermum copticum harvested in Yazd province are much higher than those found in Trachyspermum copticum harvested elsewhere.

Keywords: Trachyspermum Copticum, Therapeutic Effects, Seed essence, Antioxidant, Antimicrobial, Active ingred

Circular RNA hsa_circ_0003227 may serve as a diagnostic marker for breast cancer (Research Paper)

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Introduction: Circular RNAs (circRNAs) is an emerging type of ncRNAs without protein translation capacity . CircRNAs is characterized by covalently closed loops without 3'- and 5'- end, which is absolutely different from linear RNA [9]. Compared to microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), circRNAs have more stable construction and sequence conservation to resist the digestion of enzyme. Thus, circRNAs could much easier to be accumulated in cytoplasm or interstitial fluid, presenting higher concentration than corresponding linear RNAs. Emerging evidence suggests that the biological functions of circRNAs including serving as ceRNAs or miRNA sponges, interacting with proteins , regulating gene transcription and translation, suggesting that circRNAs will be novel biomarkers and targets for the diagnosis and prognosis of diseases. Increasing evidences have indicated that circRNAs take part in the regulation of tumorigenesis, including genesis, differentiation, migration and metastasis . It is vital to understand the molecular pathways involved in the pathogenesis of proliferation and progression . The circular RNAs can be easily detected due to their relative stability , widespread expression, and abundance in exosomes, blood, and saliva; thus, circular RNAs have potential as new and ideal clinical biomarkers in cancer.

Methods: In this study, the expression of hsa_circ_0003227 for the first time in the blood of patients with breast cancer, before and after chemotherapy was evaluated .The blood samples from 30 breast cancer patients before and after chemotherapy were collected; total RNA was extracted using Trizol and subsequently synthesized cDNA corresponding to circular RNA. Then, appropriate circular RNA primers were designed and SYBR Green real-time RT PCR was performed to evaluate the expression of circRNA in the presence of beta-actin as an appropriate internal control. The data statistically evaluated using Graph Pad Prism 8.2 software.

Results: The expression level of hsa_circ_0003227 in the blood sample of patients with breast cancer before chemotherapy has increased compared to the normal blood sample and also its expression in the blood sample of patients after chemotherapy has decreased compared to before chemotherapy.

Conclusion: The data revealed that hsa_circ_0003227 could potentially be proposed as a prognostic biomarker for breast cancer. Advanced related research in this field may be promising in cancer management.

Keywords: circRNA , breast cancer , hsa_circ_0003227, biomarker, Biological diagnosis, Noncoding RNA

Circulating RNAs as promising diagnostic biomarkers for endometriosis (Review)

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Introduction: Endometriosis is one of the common gynecologic disorders at the reproductive age of women, which can lead to infertility and pelvic pain. The diagnosis of endometriosis remains invasive, thus a reliable non-invasive biomarker or panels of biomarkers are urgently needed. To this end, circulating RNAs including miRNAs and mRNAs have been studied as peripheral blood biomarkers in affected individuals. In this review, the latest results of these studies are provided, which suggest expanding studies concerning serum or plasma biomarkers for the diagnosis of endometriosis.

Methods: The research and review papers between 2000 and 2020 were selected from Pub Med, Scopus and Google scholar databases, aiming to evaluate the effectiveness of peripheral blood biomarkers for endometriosis.

Results: The studies showed that there was an aberrant expression of miRNAs in serum or plasma of patients with endometriosis. Also, they suggest a panel of five miRNAs, which can distinguish between women with endometriosis and control women. On the other hand, some results demonstrated altered expression of VEGF and Survivin genes as diagnostic significance for endometriosis.

Conclusion: Due to importance of miRNAs and mRNA as a non-invasive diagnostic biomarker in endometriosis, the expanding of studies concerning the expression of important genes, which are involved in the pathogenesis of endometriosis, in peripheral blood or evaluation panel of important altered expression of miRNAs and mRNAs may be useful to consider as biomarkers for detecting endometriosis non-invasively.

Keywords: endometriosis; blood; biomarker; mRNA; non-invasive; miRNA

Clinicians' and Midwives' Views of Factors Influencing Decision-making for Vaginal Birth after Caesarean Section: A Qualitative Study (Research Paper)

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Introduction: Caesarean section (CS) rates are increasing in both developed and developing countries. Vaginal birth after cesarean (VBAC) is an important option for reducing the CS rate.The purpose of this study is to explore clinicians' and midwives' views of factors influencing decision-making for VBAC based on the theory of planned behavior.

Methods: This qualitative study was carried out in Urmia- Iran, during 2017-2018. Data were collected using in-depth semi-structured interviews with 21 obstetricians and midwives. Participants were selected among governmental hospitals through purposeful sampling until data saturation was reached. Data were analyzed through a directed content analysis approach using the MAXQDA software version 10.

Results: Three themes and seven sub-themes including 1. "attitude toward VBAC": positive attitude and negative attitude; 2. "control belief": organizational support, fear, and self-efficacy; and 3. "subjective norms": peer recommendation and maternal perceived pressure were emerged from data analysis.

Conclusion: Clinicians' and midwives' positive attitude and clinicians' self-efficacy could reinforce their intentions to select VBAC and support the mother. Insufficient organization support, clinicians' and midwives' negative attitude, clinicians' and women's fear, clinicians' peer recommendation and pressure of outside sources, which is perceived by mothers, could be barrier factors for VBAC.

Keywords: Vaginal birth after cesarean, cesarean section, clinicians, midwives, delivery, qualitative research

Cloning and expression of influenza A virus recombinant Noraminidase antigen for use in diagnostic tests (Research Paper)

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Introduction: During the last few years, Highly Pathogenic H5N1 Influenza (HPIV) Virus other than human mortality, has created losses in the poultry industry and causes seasonal epidemics, deaths and extensive economic damages annually. So we should have diagnostic tests to control influenza infections, research on diagnostic tests containing virus proteins that have conserved sequences is always needed to elicit effective and cross-immune responses against different virus subtypes. Neuraminidase Protein(NA) is one of the influenza virus conserved proteins that can trigger a sufficient host immune response.

Methods: Bioinformatics studies on the amino acid sequence of the protein have shown that NA protein, has physico-chemical feature and contains immunogenic epitopes that can be the targets of stimulate humoral immune system. So , NA protein can be an appropriate candidate for diagnostic tests development. In this study, cloning and expression of the influenza (A/Indonesia/5/2005(H5N1) virus's NA protein in the prokaryotic host (Escherichia coli) was investigated for using in the diagnostic tests production. Thus, the NA gene fragment was amplified by polymerase chain reaction (PCR) process with designed primers. After enzymatic digestion, the gene fragment was cloned into pET21a; an expression vector, transferred to a replication host (Top10f'), and after confirmation of cloning accuracy, pET21-NA gene structure was transferred to an expression host (BL21). The NA protein expression with IPTG inducer was determined by SDS-PAGE and Western blotting using initial Anti-His6 antibody.

Results: The expression was optimized under conditions: 0.5 mM IPTG inducer at 37°C in over night. This method provides us a significant amount of NA protein (H5N1)in a short time for future purposes and demonstrates the efficient production of recombinant protein in the prokaryotic system for using in the diagnostic tests influenza infection.

Conclusion: Our data and western blot analyses showed that recombinant noraminidase has potential to be efficient production in the prokaryotic system for using in the diagnostic tests influenza infection.

Keywords: Nueraminidase , Prokaryote System, Diagnostic tests, Influenza A(H5N1)Virus

Combination of Zerumbone with 5-FU for More Effective Colorectal Cancer Treatment (Research Paper)

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Introduction: Colorectal cancer is the third most common cause of cancer-related mortality in the world. Despite conventional therapies, survival time in the advanced stages of the disease is still very low. Chemotherapy resistance is one of the leading causes of death in patients with colorectal cancer. Chemotherapy based on 5-fluorouracil is the only first-line drug for the treatment of colorectal cancer that causes therapeutic limitations due to drug resistance. Chemical resistance is mainly associated with the change in the status of cancer cells from epithelial to mesenchymal (EMT). Overcoming resistance to treatment is one of the most important challenges in the treatment of cancer patients. Herbal remedies, including herbal derivatives, are widely used to treat various cancers. Zerumbone is a promising herbal compound that is widely used to treat a variety of tumors. The use of herbal supplements that do not have specific side effects can be effective in increasing the response to treatment and overcoming resistance to chemotherapy through the synergistic effect of chemical drugs and by targeting similar mechanisms. Therefore, the aim of this study was to investigate the effect of Zerumbone on the sensitization of cancer cells in response to 5-FU drug and the use of this compound in combined cancer treatment regimens.

Methods: The cytotoxic effects of ZER and 5-FU alone or 5-FU combined with ZER on the SW48 and HCT-116 cells were determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide. The mRNA and protein level of β-catenin, Survivin and Vimentin were measured in 5-FU, ZER, 5-FU+Zerumbone treated CRC cells using RT-qPCR and western blot.

Results: Our results demonstrated that proliferation of HCT-116 and SW48 cells that were treated with ZER ,5-FU and 5-FU+ZER was significantly reduced compared to controls. Furthermore the Gene and protein expression level of Survivin, Vimentin and β-catenin in our treatment groups were significantly reduced compared to control groups. ZER and 5-FU treatment sometimes have a strengthening effect on each other and in some cases reinforced each other's unresponsiveness. Therefore ZER treatment could increase 5-FU sensitivity in CRC chemoresistance cells, which is represented that the therapeutic potential of ZER alone and together with 5-FU could be a promising therapeutic strategy in

overcoming chemoresistance, a strategy that may ultimately be applicable to other human tumors in future as well.

Conclusion: Regarding to the importance of cancer chemotherapy resistance which reduces patient response and consequently increases the risk of progression, the herbal supplements with minimum side effects can be effective in enhancing the response to treatment. Synergistic and potentiating effect of combination therapy using herbal and chemical drugs can improve patient response. Therefore, here we aimed to investigate the effect of ZER on the sensitization of cancer cells to 5-FU by evaluation of expression of main genes involved in major cellular processes.

Keywords: Colorectal cancer (CRC), Zerumbone (ZER), 5-Fluorouracil (5-FU), Chemotherapy

Combined Growth Factor and Gene Therapy: An Approach for Hair Cell Regeneration and Hearing Recovery (Review)

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Introduction: Fibroblast growth factor, nerve growth factor neurotrophins, and insulin-like growth factor 1 are considered 3 families of growth factors that can be involved in the process of otic neurogenesis. In this respect, otic neurons can also be connected with mechanoreceptors in the ear, the hair cells (HCs), as well as the central nervous system. As a growth factor is combined with gene transfer technology, it can be used for hair cell regeneration. Gene therapy can be similarly employed to introduce genes into a system in order to induce the expression of genes for therapeutic agents, to replace defective genes, or to re-program supporting or surrounding cells to acquire the phenotype of lost or damaged cells in order to repair or regenerate the damaged tissue. The purpose of this review article was to investigate the epigenetic and growth factors involved in the differentiation pathway of embryonic stem cells (ESCs) into HCs and auditory neurons (ANs).

Methods: To this end, the databases of Directory of Open Access Journals, Google Scholar, PubMed (NLM), LISTA (EBSCO), as well as Web of Science were searched.

Results: : Given the results available in the related literature, the differentiation efficacy of ESCs toward the ANs and the HCs, the important role of growth factors, and 3 different strategies of application of miRNA, epigenetic regulation, and preparation of three-dimensional (3D) environments were suggested to be taken into consideration in order to improve these studies in the future. Furthermore, the role of epigenetic mechanisms and miRNA in this differentiation process became quite obvious; hence, the utilization of such procedures in the near future would be significant

Conclusion: Combining several techniques with a synergic effect (such as growth factor gene therapy and 3D environments) seemed to lead to obtaining the best results as a therapeutic strategy.

Keywords: Growth factor · Three-dimensional culture system · Hearing loss · Hair cell regeneration · MicroRNAs

Comparative investigation of effects of the agricultural pesticides (diazinon and chlorpyrifos) on spermatogenesis in BALB/c male mice (Research Paper)

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Introduction: Diazinon and chlorpyrifos are kind of organophosphate toxins used for agricultural pests. These toxins control acetylcholine Enzyme and heart cells and reproductive system. It also cause infertility. Because of using a lot of these compounds in rice fields and citrus trees specially in north of Iran, we tried to compare effects of diazinon and chlopyrifos on sex hormones and spermatogenesis trends in BALB/c male mice.

Methods: Including control, 60 male mice devided into 6 groups (with ten in each) including sham, control and experimental mice (dose of 27.2 , 40.8 mg/kg for chlorpyrifos toxin and dose of 40 and 60 mg/kg for Diazinon). Experimental groups receive diazinon and chlorpyrifos intraperitoneally for 35 days with two days of rest diluted water inject to sham group. There aren't injection for and blood was taken for test stron evaluation next, epididim extracted for determining motility and number of sperm. They embed on HTF medium. Testis evaluated for producing sections and studding different cell classes. They evaluated with use of SPSS software and tukey test and one-way variance analysis ($P<0.001$, $P<0.05$). Finally the chartdrew by Excel software.

Results: With use of microscopic evaluation, it is determined that number of spermatozoids cells, Spermatids Certoli and semmiferous tubules and diameter of seminiferous tubules have significant decrease ($P<0.001$, $P<0.05$) Also, the number of leydig cells decrease significantly with comparison to control and sham groups. Then testostron hormones decrease sperm comparison of experiment and control groups showed that diazinon and chlorpyrifos as environmental factors may affect significantly on sperm and producing sex hormones parameters.

Conclusion: Falling seminiferous tubules which are necessary for producing sperm can increase probability of infertility. In comparison to chlorpyrifos toxins, Diazinon has more negative effects. This study suggests more attention to suitable management of using this toxins.

Keywords: pesticides, diazinon, chlorpyrifos, spermatogenesis, male mice

Comparative study of liquid overlay and hanging drop techniques in MCF-7 spheroids. (Research Paper)

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Introduction: Breast cancer is the most common cause of cancer in women. It is becoming recognized that two-dimensional (2D) cell cultures do not accurately reflect the conditions in vivo. Cell-cell and cell-matrix interactions cannot be imitated via 2D cell cultures. To overcome these limitations, three-dimensional spheroid culture models have developed.3D models can simulate the function of living tissues. In this study, we indicated the generation of MCF-7 spheroids.

Methods: We used hanging drop and liquid overlay techniques for generation of MCF-7 spheroids.In liquid overlay technique, the bottom of the cell culture plate was coated with agarose in order to provide non-adherence surface. Cell suspension was loaded in to plate. In hanging drop method, cells were suspended in drops on the inverted lid of the petri dish. Drops were incubated until spheroids were formed. Wells of the 96 culture plate were layered with agarose and each drop was loaded into one well.

Results: MCF-7 spheroids were generated in both techniques. Spheroid formations occurred within 96h in Liquid overlay and 48h in hanging drop method. Volume and shape of spheroids were not same in liquid overlay technique but uniform-sized spheroids were observed in hanging drop technique.

Conclusion: Three- dimensional cell cultures mimic tumor microenvironment. Since hanging drop method can generate uniform-sized spheroids, it is more useful to form MCF-7 spheroids. This technique can be used in different studies such as cell behaviors, drug screening and gene expression.

Keywords: Three- dimensional cell culture,liquid overlay technique, hanging drop technique,MCF-7 spheroid.

Comparison of the antibacterial effect of aqueous extract of Teucrium polium with the Chlorhexidine mouthwash on Streptococcus mutans (Review)

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Introduction: The treatment of tooth decay increases the likelihood of allergic reactions and bacterial resistance to antibiotics. Effective compounds of medicinal plants can be effective in preventing oral diseases. Teucrium polium is one of the native plants of Iran that has been found in Khuzestan province and despite its enormous therapeutic applications, it is not well known. The aim of this study was to investigate the antibacterial effect of Teucrium polium on Streptococcus mutans and compare it with the Chlorhexidine mouthwash.

Methods: In this study, aqueous extraction was acquired by the hot extraction method. The antibacterial effects of the extracts were investigated by two methods of broth microdilution to find the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the aqueous extract and the disk diffusion method on bacteria in comparison with the Chlorhexidine mouthwash.

Results: MIC and MBC for aqueous extract of Teucrium polium were 15.63 and 31.25 mg/ml, respectively. The diameter of Streptococcus mutans non-growth halo in the vicinity of the Chlorhexidine mouthwash disk with the concentration of 0.2 mg/µl was 13 mm and adjacent to the disk of Teucrium polium extract with two concentrations of 20 and 5 mg/µl were 10 and 8 mm, respectively.

Conclusion: The findings of this study showed that the aqueous extract of Teucrium polium has effective antibacterial activity on Streptococcus mutans, although the effect of the Chlorhexidine mouthwash is significantly higher than the aqueous extract of this plant. Due to the availability and nativeness of this plant in Iran and the possibility of using it with lower costs and complications than the Chlorhexidine mouthwash, the use of this plant extract in mouthwashes can be very efficient and useful.

Keywords: Prevention of tooth decay, Streptococcus mutans, Medicinal plants, Teucrium polium, Chlorhexidine

Comparison of the effect of Brassica oleracea and letrozole on aromatase inhibitor enzyme and steroid hormone levels and oocyte development in Trichogaster trichopeterus (Research Paper)

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Introduction: Today, traditional medicine and the use of herbal extract have found a special place among the patients. The abundance and the ease of availability of the Brassica oleracea has made it popular in some countries. Recent analyzes on the compounds found in Brassica Oleracea has shown a magnificent effect on the ovary, pituitary-gonadal axis and aromatase inhibitor. Therefore, further researches can be done in order to use this plant instead of Letrozole (as a chemical drug) in the treatment of metastatic breast cancer in postmenopausal [1,2,3].

Methods: In this research,120 female fish speciments of Trichogaster trichopterus with average weight of (3-4) grams in 9 treatments were divided into control groups,control1 (intact) and control2 (ethanol injection) and control3 (normal saline injection) and treatment groups receiving 200, 400, 800mg / kg alcoholic extract of Brassica oleracea and 0.1, 0.5 ,1 mg /kg of letrozole. All the prescriptions were administered 10 times in 3 replicates one day in between in intramuscular (IM) injection within 20 days. At the end of the experiments, the fish were anesthetized with clove extract , ovarian histology and sex hormones and liver enzyme were studied in treatments and were compared with control groups.

Results: The statistical results of the level of sex hormones liver enzymes showed significant differences between in the controls groups and treatments ($P<0.05$). Also the results of this research showed the inhibitory effect of Brassica oleracea extract and letrozole on oocyte maturation in mature female three spot Gourami.

Conclusion: The result of this study showed that extract of Brassica oleracea such as letrozole can inhibits aromatase enzyme and barrier of oocyte maturation in female three spot Gourami. letrozole can increases the liver enzymes and changes in fat cells but Brassica oleracea decreases the liver enzymes.

Keywords: Brassica oleracea, letrozol, Trichogaster trichopterus, ovary, liver

Comparison of the Effectiveness of High Intensity Intermittent and Continuous Moderate Exercises in Weight Loss Process (Review)

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Introduction: Background and purpose: Obesity is one of the most common diseases and one of the major causes of mortality worldwide, which is known as abnormal or excessive accumulation of fat in the body which disrupts one's health. Physical activity and exercise play an important role in the prevention and treatment of obesity, and various types are suggested in terms of type, severity and duration. The purpose of the present study is to evaluate and compare the effectiveness of high intensity and moderate intensity continuous exercise in weight loss process

Methods: Search Method: Searches in various databases such as PubMed, Scopus and Sciencedirect with keywords such as overweight, obesity, high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT)

Results: Results: Some studies show that HIIT training has a greater effect on reducing body fat compared to MICT training, which increases cardiac output and improves cardiac performance. In some other studies, however, both types of exercise have had approximately the same effect on weight loss and body fat as well as on decreasing inflammatory factors such as TNF-α, although HIIT exercises require approximately 40% less time. Exercise programs that include running have also been shown to be more effective in inducing changes in body composition, while cycling exercises have been less effective

Conclusion: Conclusion: According to the results of the studies, it seems that using HIIT exercise due to its good effect on weight loss and less time required and due to lack of time which is a reason for many people to not participate in exercise programs. Together with diet therapy can be a new and appropriate approach for the prevention or treatment of overweight and obesity

Keywords: Keywords: Obesity, Overweight, High Intensity Intermittent Exercise, and Medium Intensity Exercise

Complementary and alternative medicine in infertility (Review)

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1. Dr.

Introduction: Although there is little information available to quantify the use of complementary and alternative medicine (CAM), growing evidence suggests that CAM prevalence among patients seeking infertility treatment is increasing worldwide. The aim of the present study is to review studies focused on Complementary and alternative medicine in infertility.

Methods: Comprehensive searches of peer-reviewed papers were conducted via databases including Google scholar, PubMed, Science direct, and ISI Web of Science; from 2009 to 2019. A comprehensive set of search terms was used to avoid missing potentially relevant material. Only published articles that were available in English, qualitative or quantitative, RCT, quasi clinical trial or longitudinal and focused on complementary and alternative medicine in infertility were included. Studies excluded if they were not population-based and non-English.

Results: 62 papers were found in the first step and finally 14 of them extracted based on relevancy to the topic. Herbs and spiritual healing are widely used among patients in adjunct to conventional medical interventions. Most studies assessed a variety of CAM modalities met inclusion criteria. Several studies that focus on acupuncture, selenium supplementation, weight loss and psychotherapeutic intervention showed beneficial effect but more interventions had been studied less and evidence for them was limited. Cultural beliefs regarding using CAM by infertile patients showed participants' CAM use was consistent with cultural traditions of health and fertility: Westerners relied primarily on biomedicine and used CAM mainly for relaxation, whereas non-Westerners' CAM use was often influenced by culture-specific knowledge of health, illness and fertility.

Conclusion: Although there is preliminary evidence of the effectiveness of some CAM interventions among infertile patients, many of these interventions require further investigation before they can be considered for routine clinical use. As CAM use is prevalent among patients, there is a clear need for health providers to become more aware of this phenomenon and for further research in this field.

Keywords: Complementary Medicine, Alternative Medicine, Infertility

Comprehensive Review of Cinnamon's Effects on Cancerous Tumors (Review)

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Introduction: Nowadays Cancer is one of the Most Common Causes of Death Around the World. Cancer Results from the Uncontrollable Growth of Cells Following a Mutation in the DNA. This Mutation can Result in Proto-Oncogenes Turning into Oncogenes and Subsequently an Alteration in their Translations. In addition, the Missing Apoptosis, the Death of Cells, can Result in Cell Multiplication and Eventually Turn a Normal Cell into an Acute Multiplying Cell. Considering the high Mortality Rate Attributed to this Disease Globally, There have been Numerous Studies of the Effects of Herbal Medications with the Goal of Stopping or Impeding the Uncontrolled Growth of Cells. Cinnamon has Received a lot of Attention from the Scientific Communities Around the World due to Some Anti-Cancerous Properties and Containing Cinamaldehyde, Eugenol, Coumarin, Cinnamic Acid and Hydroxycinnamaldehyde Compounds.

Methods: In the Current Literature Review Key Words Including Cinnamon, Tumor, Cancer, Coumarin and Cinamaldehyde from the List of MeSH and other Credible Scientific Websites such as Science Direct, PubMed and Google Scholar were Reviwed and Used to Compile the Effects of Cinnamon on Cancers and Tumors.

Results: A Large Body of Research has Found that Cinnamon can Hinder Angiogenesis and Boost the Activity of CD8+ Cells, which can in Turn Hinder the Growth of a Cancerous Cell. In addition, Cinnamic Acid can Impede Lung Adeno Carcinoma, Hinder the Proliferation of Cancerous Lung Stem-Cells, Increase of Apoptosis Among Cancerous Liver Cells, and Activate Caspase-3 and the Impeding JAK-STAT Signal. Hydroxycinnamaldehyde Compounds can also Prevent the Metastasis of Lungs and Increase the Transcription of Cadherin-E Proteins

Conclusion: The Studied Journals Indicated the Positive Effects of Cinnamon on Cancerous Tumors and its Impact on Regulation of Cell Growth Cycles and Impediment of Uncontrolled Cell Growth

Keywords: Cinnamon, Tumor, Cancer, Coumarin, Cinamaldehyde

Comprising clinical symptoms and paraclinical findings in Alzheimer's disease and Dementia with Lewy bodies: a cross-sectional study. (Research Paper)

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Introduction: Background: According to studies, many similarities in the clinical symptoms of Alzheimer's disease (AD) and Dementia with Lewy bodies (DLB), in many cases lead to a misdiagnosis. Therefore, recognizing the symptoms of these two diseases and their diagnostic differences can be very important. Purpose: Therefore, the purpose of this study was to evaluate and compare symptoms of AD and DLB for early differentiation of them.

Methods: In this cross-sectional study, 80 patients from 22 Bahman hospital in Mashhad and a private neurology clinic, according to the met criterion of DSM 5th edition, enrolled in the study in 2016 to 2019, were divided into two groups of 40 patients (with DLB and AD). Demographic indicators, disease history, underlying illnesses, previous medication, clinical signs of patients, were completed in the checklist. Patients diagnosed with other subtypes of dementia, Parkinson's disease, depression, and using sedative or other drugs that affect cognitive impairment were excluded from the study. To determine cortical atrophy, MRI imaging of each patient was performed.

Results: The results showed that there was no significant difference between the two groups in terms of age, sex, marital status, and occupational status (P-value> 0.05). The onset of symptoms in patients with AD was sooner than that of patients with DLB. Also, the duration of diagnosis in DLB was significantly faster than AD (P-value = 0.001). In patients with DLB, symptoms of visual hallucinations, bradykinesia, and cognitive fluctuations were significantly higher than those of patients with AD (P-value <0.05). Also, the results showed that there was no significant difference between the two groups in terms of underlying diseases such as diabetes, hypertension, and hyperlipidemia (P-Value> 0.05). The results of the imaging showed that there was no significant difference between the two groups in terms of the cortical atrophy results (P-value = 0.481).

Conclusion: For differentiation between the two subtypes of dementia, Dementia with Lewy bodies and Alzheimer's disease, we observed on the same timeline that DLB was diagnosed earlier than AD; symptoms of hallucination, cognitive fluctuation, and bradykinesia is strongly aiming to dementia with Lewy bodies.

Future studies need to consider more paraclinical tests and exact tests for clear results.

Keywords: Alzheimer's disease, Dementia with Lewy bodies, Clinical symptoms, Differentiate.

Concomitant use of heat-shock protein 70, glutamine synthetase and glypican-3 is useful in diagnosis of HBV-related hepatocellular carcinoma with higher specificity and sensitivity (Research Paper)

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Introduction: Hepatocellular carcinoma is the third leading cause of cancer-related death worldwide and late diagnosis is the main cause of death in HCC patients. In this study expression patterns of HSP70, GPC3 and GS and their relationships with pathogenesis of HCC in Iranian patients were investigated.

Methods: The expression of HSP70, GPC3 and GS were determined by immunohistochemistry and quantitative real-time PCR (q-PCR) methods, using 121 cases from patients with HBV alone, HCC without HBV, HBV+HCC and 30 normal tissues as control group.

Results: HSP70, GPC3 and GS were expressed in higher levels in HBV-related HCC samples compared to HBV alone group. The results showed that the labeling index of HSP70, GPC3 and GS are correlated with immunohistochemical and molecular expressions of HSP70, GPC3 and GS. The sensitivity and specificity for HCC diagnosis were 43.4% and 89.7% for HSP70, 64.3% and 90.4% for GPC3, and 60.7% and 94.3% for GS, respectively. The sensitivity and specificity of the panels with 3, 2 and 1 positive markers, regardless of which one, were 21.6% and 100%, 51.3% and 100% and 93.4% and 80.5% respectively.

Conclusion: The current study demonstrated an association between HSP70, GPC3 and GS expressions and HBV-related HCC in our population. It was concluded that HSP70, GPC3 and GS expressions could be useful biomarkers for increasing the specificity and sensitivity of HCC diagnosis to acceptable level. Also, proper combinations of these 3 markers could improve diagnostic accuracy.

Keywords: GPC3; GS; HSP70; hepatocellular carcinoma; immunohistochemistry; quantitative real-time PCR..

Consequences of Women's Empowerment: A Review of the Literature (Review)

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Introduction: Women's empowerment is one of the topics that has received more attention in advanced societies because half of the population is women. Studies show that women's empowerment has many consequences on family health. As women's role in family health and empowerment is one of the essential aspects, the present study was conducted with the aim of reviewing the consequences of women's empowerment.

Methods: The present study is a review study. In this study, the researcher conducted a comprehensive search of databases in Google Scholar, SID, PubMed, Scopus, Cochrane library and up to date, employing English keywords combination of Empowerment, Women's Empowerment, Family Health, Education Empowerment, Social Empowerment, Economic Empowerment, Policy Empowerment, Culture Empowerment, Psychological Empowerment and their Persian equivalent. Overall, 170 articles were obtained from 2000 to 2020. Then, 84 of these articles due to duplication, 26 articles due to irrelevance, 13 articles in the abstract screening stage, and 4 articles in the full-text review stage were deleted. Finally, 43 articles were used for writing.

Results: The present study's findings are reviewing the consequences of women's empowerment were divided into five general categories: Psychological consequences category including (feeling of worth, intellectual independence, self-efficacy, positivity, sense of power, self-esteem, and self-efficacy), Social consequences includes (increased participation in social affairs, increased social support, increased education), Economic consequences included (employment and increased access to resources and financial support), Cultural consequences included (change of traditional beliefs), Reproductive health category included (improving fertility behaviors, increasing the power to decide on the number of children, the age-differences between children, methods of contraception, and reducing domestic violence).

Conclusion: Considering the critical role of women in family health and the importance of women's empowerment and since women's empowerment is associated with many consequences on women and consequently on family health, it is recommended to plan, train and implement effective interventions by providing healthcare providers have taken an important step towards promoting women's empowerment, family and community health.

Keywords: empowerment, women's empowerment, family health

Construction of Designed Expression Vectors for Analysis of Reciprocal Interactions Between RAX And E2F1 Transcription Factors in HEK-293T Cells (Research Paper)

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Introduction: Vision is one of the vital senses of human beings that is involved in most of the daily activities of life. Retinal Progenitor Cells (RPCs) are multipotent progenitors derived from retinal stem cells, with the potential to be differentiated into various types of retinal cells. Previous studies have demonstrated that retinal development is controlled by coordinated interactions between three key groups including transcription factors, cell cycle components, and regulators of signaling pathways. Hence, it is important to identify regulatory interactions between these components. E2F family, are conserved transcription factors (TFs) with dual activities like a double edge sword in different biological process and play roles in both proliferation and apoptosis. This family is divided into three groups including activators (E2F1, E2F2, and E2F3), repressor (E2F4, E2F5, and E2F6), and atypical groups (E2F7 and E2F8). E2F1, A member of the activator group, is a crucial player involved in cell cycle progression from G1 to S phase by binding to the promoters of target genes and induction of their transcription. Homeobox genes are a group of transcription factors that are critical for the development of many organs, including brain and eye of vertebrates. Retina and anterior neural fold homeobox (RAX) is one of the important Homeobox genes with significant roles in the forebrain and eye development of vertebrates. RAX expression leads to commitment of retinal progenitor cells by regulating their initial specification and proliferation. It has been shown that knockout of RAX gene in mice led to no eye formation and also abnormal formation of the forebrain.

Methods: Bioinformatic studies have predicted several binding sites of E2F1 approximately within 3 kb upstream of human RAX gene. Furthermore, based on in silico analysis, a 1658 bp fragment upstream of the human E2F1 gene was considered as E2F1 promoter. The coding sequences of RAX and E2F1 and also regulatory region of E2F1 gene were amplified by PCR. These segments were then cloned into target expression vectors harboring EGFP and mCherry reporters, which later was used for monitoring of transcription factor plasmids transfection. Next, the effect of E2F1 transcription factor on RAX promoter activity and the putative reciprocal interaction of RAX protein with E2F1 regulatory region were

evaluated by transient transactivation assay in HEK-293T cells. For this purpose, target expression vectors were transfected into HEK-293T cells using lipofectamine LTX reagent.

Results: Results: The integrity of the expression vectors were also examined by restriction digestion and PCR. Prior cloning into the expression vectors, the accuracy of the amplified sequences were also confirmed by sequencing analysis. The results indicated that all target fragments were inserted into mammalian expression vectors. The successful expression of EGFP in HEK-293T cells was confirmed by microscopic analysis. 48 h post co-transfection of vectors which were target promoters and expressing TFs, cells were lysed, total RNA was extracted and incorporated in cDNA synthesis. In order to investigate the interaction of RAX and E2F1, the level of EGFP mRNA derived by target promoters were analyzed using q-PCR.

Conclusion: Conclusion: Retinal degeneration is an irreversible condition in which progressive death of retinal cells leads to deterioration of the retina. As E2F1 and RAX are critical modulators of RPC proliferation, analysis of their interactions might provide better insight into the mechanisms underlying retinal progenitor maintenance which is important to have better therapeutic approaches in regenerative medicine for treatment of retinal degenerative disease. This study aimed to evaluate the mutual interactions between RAX and E2F1. Construction and transfection of vectors expressing RAX and E2F1 CDS and promoters into HEK-293T cells were successfully accomplished, and in vitro evaluation of interactions between these two transcription factors were studied by EGFP expression analysis using q-PCR.

Keywords: Retina Progenitor Cells, Transcription Factor, E2F1, RAX, Proliferation

Contribution of Iran in Alzheimer's Disease Research during 2010-2019; A Scientometric Analysis (Research Paper)

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Introduction: Alzheimer's disease is the most prevalent form of dementia and is a rising issue for global health. Due to the necessity of research to better address this important neurological disorder, this study was established aiming at reviewing Alzheimer's disease scientific publications by Iranian researchers.

Methods: The search process was performed on 28 Aug 2020. We searched for Alzheimer and all its related keywords in the Web of Science (WoS) database to find documents published by Iranian researchers from 2010 until 2019. Bibliographic parameters were assessed. The co-authorship matrix was calculated using Bibexcel, and visualizations were performed by VOSviewer.

Results: A total of 1042 documents from 4949 researchers (4.7 authors per document) were retrieved from WoS. Original articles [804(77.1%)] and reviews [169(16.2%)] were the most common types for Iranian publications and also one article was retracted. In terms of the number of publications, Iran ranked 20th in the WoS database. Time trend analysis demonstrated an ascending growth of publications in the field of Alzheimer's disease among Iranian researchers. Tehran University of Medical Sciences was the pioneer organization with 286 records (27.4%). The authorship distribution pattern revealed that 59.2% (617) of documents were written in small groups (1 to 5 authors). In results, Khodagholi F. with 57, Foroumadi A. with 48, and Nadri H. with 45 documents were the most active Iranian authors. The average citation per document was 20.68 (h-index=50). The European Journal of Medical Chemistry published the highest number of documents from Iranian authors in the field of Alzheimer's disease. Iranian authors mostly collaborated with researchers from the United States, Italy, Australia, and Canada, respectively. The co-occurrence network for keywords represented five publication clusters in the collection. The largest cluster was related to oxidative stress in Alzheimer's disease, followed by in-vivo studies in the field of brain neurons destruction.

Conclusion: Iranian researchers made significant contributions in the field of Alzheimer's disease during 2010-2019 and covered a wide range of Alzheimer's disease-related areas over the last decade. Also, based on Iran's publication rank

in WoS, further research and contributions can be conducted by Iranian researchers.

Keywords: Tauopathy, Dementia, Alzheimer, Scientometrics, Publications

Controlled Delivery of Brain Derived Neurotrophic Factor and GoldNanoparticles from Chitosan/TPP Nanoparticles for Tissue Engineering Applications (Research Paper)

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Introduction: Brain derived neurotrophic factor (BDNF) is highly effective in the treatment of various diseases, and selected for growth factor delivery system. Also, gold-nanoparticles (AuNPs) plays the paramount role in diagnosis and treatment of diseases.

Methods: The aim of this study is to encapsulate BDNF and AuNPs in chitosan nanoparticles and its effect on human adipose derived stem cells (h-ADSCs) proliferation was evaluated. The ratio of 1:3 chitosan/TPP was determined as the optimum ratio, BDNF or AuNPs were added to 0.1% chitosan solution for preparation of nanoparticles. The release rate of BDNF and AuNPs were assessed by Bradford test and inductive coupled plasma optical emission spectrometry technique, respectively.

Results: In this study, BDNF and AuNPs loading efficiency were 89.46 ± 2.77 (%) and 93.8 ± 2.12 (%), respectively. The kinetic release of BDNF is 83.28 ± 2.22 (%) and AuNPs release rate was 48.4 ± 0.108(%), during the 7 days. MTT findings demonstrated h-ADSCs viability in the presence encapsulated BDNF and AuNPs is significantly more than control group on 3 and 7 days

Conclusion: These findings indicate the controlled release of encapsulated BDNF and AuNPs, and synergist effects of nanoparticles on h-ADSCs viability; it suggests an efficient delivery of BDNF and AuNPs, for tissue engineering.

Keywords: BDNF , Chitosan, Delivery system, Gold nanoparticle, Controlled release

Correlation of Resistin Serum Level with Fat Mass and Obesity-Associated Gene (FTO) rs9939609 Polymorphism in Obese Women with Type 2 Diabetes (Research Paper)

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Introduction: The aim of this study was to detect any association of fat mass and obesity-associated (FTO) rs9939609 variant to metabolic and anthropometric parameters and resistin level as adipokines in Iranian obese women with type 2 diabetes mellitus.

Methods: Totally, 42 diabetic and 36 nondiabetic women were selected. The PCR amplicons of FTO gene were sequenced and metabolic, anthropometric parameters and resistin levels were measured.

Results: Serum resistin concentrations were not different between diabetic and non-diabetic subjects ($p > 0.05$), while resistin level in diabetic group with AA genotype was lower than that with other genotypes in the same group. In rs9939609 SNP adjusted analysis, insulin and HOMA levels were high in AA genotype. While levels of FBS and HbA1c were higher in AA and AT genotypes. In diabetic group, only TG showed significant difference among three genotypes and mean of TG was higher in TA genotype. No significant correlation between resistin and anthropometric and metabolic parameters was found except for DBP in diabetic patients.

Conclusion: There was no significant association between rs9939609 and resistin serum level in type 2 obese diabetic women while percentile ranges (25th, 50th and 75th) of resistin concentrations was high in diabetic group.

Keywords: Rs9939609 polymorphism, FTO gene, Obesity, Type 2 diabetes, Resistin.

COVID-19 screening by CT scan . YES or NO ?! (Review)

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Introduction: COVID-19 was declared an epidemic on March 11, 2020 by the World Health Organization. In the absence of drug intervention as well as the lack of an effective vaccine against COVID-19 , the only solution against the disease is to separate susceptible and diseased individuals by finding a safe and convenient screening method. From the earliest days of COVID-19 Pandemic, CT scans have played a key role in the rapid and reliable diagnosis. In this study, we want to answer the question '' is CT scan a Reasonable method for COVID-19 screening? ''

Methods: In this review, we searched for COVID-19 screening, The role of CT scan in COVID-19, Disadvantages of CT scan, Diagnosis of COVID-19 in websites such as the Pub Med and Google Scholar. Finally, 38 papers in English and Persian were used for the regulation of the article.

Results: The present study indicates that, From the beginning of the COVID-19 pandemic, it became clear that pulmonary symptoms, including GGo(Ground-glass opacification), were the best way to diagnose the disease quickly and People who suspect COVID-19, should have a CT scan to make sure and start the treatment process. CT scan with its special features including: 97% diagnostic accuracy, Diagnosis before symptoms occur, Availability and high speed in disease diagnosis is a sensible way to diagnose COVID-19; However, There are problems with using computed tomography imaging as a screening tool. During the CT scan, the patient is given 8 mSV (unit of ionizing radiation dose in SI) for each lung CT scan. To imagine its greatness, it can be said that in a Plain radiograph of the lung, 0.02 mSV are given to the patient. Ionizing beams have many detrimental effects on body cells. They can cause cancer by damaging DNA. During a pandemic, a person may be screened several times. If we use CT scan as a screening tool, with increasing the number of CT scans, the risk of cancer increases and these complications are more severe in children and adolescents.

Conclusion: According to studies and articles, Due to the Possibility of radiation damage and non-reproducibility, CT scan is not a reasonable and safe method for screening against COVID-19 and this test should be performed only if a person is suspected of having the COVID-19 or in groups sensitive to this disease. Remember that unnecessary CT scans should always be avoided.

Keywords: COVID-19 screening, The role of CT scan in COVID-19, Disadvantages of CT scan, Diagnosis of COVID-19

COVID-19 blockers: A review of new strategy to inhibit COVID-19 invasion by peptides (Review)

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Introduction: The emerging coronavirus 2019 (COVID-19) is a very serious threat to the health of people around the world, so it is essential to search for prevention and safe and effective treatment against the acute coronavirus syndrome 2(SARS-CoV-2), which Also known as the 2019 coronavirus (2019-nCoV). The main cause of SARS-CoV-2 infection is the interaction between SARS-CoV-2 and the host surface receptor protein, the human angiotensin-converting enzyme (hACE2). Therefore, blocking the early entry of the virus can be a promising strategy/treatment to fight SARS CoV-2 infection. In this article, we reviewed several researches that investigate this issue.

Methods: The strategy used in these researches was to design specific peptides that are spatially and chemically complementary to the cell surface receptor (hACE2) or virus spike. Then, developing a computational setup to simulate molecular dynamics and calculated the binding energy. In silico and experimentally optimization of designed peptides were applied for the proper target binding, folding and stability.

Results: A number of peptides designed to block SARS-CoV-2 have been proposed. It has been shown that some of them can reduce the virus load in the cell by blocking cell surface receptors, blocking the spike of the virus particle, or preventing the virus from binding to the cell receptor at the cell entry stage.

Conclusion: Findings from the reviewed research may provide a new antiviral treatment for COVID-19, which may address the global crisis of the disease. Therefore, the results of this research can give an interesting direction to the existing prevention and treatment processes.

Keywords: COVID-19, Peptides, hACE2, SARS-CoV-2

COVID-19 Molecular Crosstalk with Prostate Cancer: Possible Therapeutic Applications (Review)

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Introduction: The universal pandemic of coronavirus disease 2019 (COVID-19), termed SARS-CoV-2 by the World Health Organization (WHO), is an illness caused by a new coronavirus.

Methods: While prostate cancer (PCa) is the second most common cancer in men worldwide, the incidence and mortality rate of COVID-19 positive prostate cancer patients are increased to 16.76% and 20%, respectively. The effective factors on the intensity of COVID-19, such as diabetes, alcoholism, hypertension, and active smoking are also known to affect the progression of prostate cancer. This crosstalk is related to potential association among SARS-CoV-2 effect on host epithelial cells and prostate cancer genetic abnormality and molecular signatures, such as AR and TMPRSS2. As the molecular mediators of SARS-CoV-2 infection, antiandrogen-converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TMPRSS2) genes are co-expressed on ciliated bronchial epithelial cells, type 2 pneumocytes and the epithelial cells of small intestine. The virus spike glycoprotein (S) is primed by TMPRSS2 protease to invade the host cells. TMPRSS2 gene is extremely identified in the male urogenital system organs, including the prostate gland.

Results: Prostate cancer treatments that target SARS-CoV-2 are considered effective when used in blend with other potential repositioned drugs that may be beneficial versus COVID-19. Anti- androgen drugs and TMPRSS2 deterrents used on prostate cancer are suggested to stimulate protective role against SARS- CoV-2 and may perform as regular therapeutic selections for COVID-19 patients. It is hypothesized that the strategy of down- regulating TMPRSS2 by androgen elimination through classical androgen-deprivation drugs (e.g. leuprolide) and oral AR signaling inhibitors (e.g. enzalutamide, apalutamide or darolutamide), that are frequently consumed in prostate cancer treatment, might also be beneficial as a treatment for COVID-19. Although it should be noted that androgen deprivation therapy (ADT) which has been safely used for extensive span, do not afford oncology benefit and can supply to immoderate morbidity or fatality.

Conclusion: Thus, due to this possible molecular crosstalk between SARS- CoV-2 and prostate cancer, it is suggested to examine the possibility of repurposing prostate cancer treatments for COVID-19, alone or in combination with other therapeutics, in order to decrease the serious side effects and increase the specificity and efficacy of treatment.

Keywords: COVID-19; SARS-CoV-2; prostate cancer; androgen deprivation therapy; TMPRSS2

Covid-19 Treatments Based on pathogenicity (Review)

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Introduction: It is important to know the mechanism by which the coronavirus enters the host cell and consequently causes infection in the host. the virus first binds to Angiotensin-converting enzyme 2 (ACE2) receptors on the surface of host cells and then enters the cell, then the virus starts proliferation, membrane fusion, assembly, and subsequent infection and cytokine secretion. By Understanding the pathogenesis stage of the virus, as well as identifying the drugs that prevent the virus from spreading in each of these stages, Controlling the disease and the recovery of patients is possible.

Methods: Article selection were conducted through advanced search in web of science, Pubmed database and without time limit, using two keywords derived from MeSH (SARS-CoV-2 and treatment) and limiting the search to keywords in the abstract. From the 40 available articles, based on the content of the abstracts, 19 articles related to treatment of SARS-CoV-2 were selected. The articles were studied and key points of each were identified.

Results: The virus is likely to infect epithelial cells in the nasal cavity even with a low load and begins to multiply.The virus travels in the respiratory tract along the airways, triggering a strong innate immune response and the disease becomes clinically apparent. about 20% of infected patients progress to stage 3 of disease and develop an infection in the alveolar cells and lung gas exchange units.Coronavirus has a number of proteins including Protein spike. Protein S contains RBD, which is the basic Ag for binding to ACE2. Overexpression of ACE2 may facilitate virus replication in lung tissue.There are various drugs for the treatment of this disease with different methods. methods such as: inhibition of some cellular receptors, prevention of virus entry, inhibition of some intracellular proteases, etc. The primary strategies involved are to prevent the binding of the SARS-CoV2 virus to ACE2 and ACE2 may be a drug target to limit the entry of the virus. SARS-CoV-2 has been shown that The process of binding of protein S to the ACE2 receptor is facilitated by host cell-derived serine protease (TMPRSS2). Kamvastat mesylate prevent SARS-CoV-2 infection and commostat mesylate

reduces its infection. SARS-CoV-2 has recently been shown to be a receptor for the ACE2 to enter the host cell from the S protein. Therefore, the ACE2 forms a molecular target to prevent SARS-CoV-2 from entering host cell. Upon entering the host cell, viral single-stranded RNA is released to amplify the RNA virus and translate the virus polyproteins. Lopinavir, Ritanovir and some are candidates for treatment. Due to anti-inflammatory activity, corticosteroids (CS) are an adjunct therapy for acute respiratory distress syndrome and cytokine storm. One of the first defense lines against RNA viruses such as SARS-CoV-2 is the release of type I and III IFNs. Recently, there has been great interest in the therapeutic effect of modulating the IFN response to inactivate the pathogenesis of COVID-19 . Excessive inflammatory responses and high levels of inflammatory cytokines including interleukins -6, 8, and 10 have been shown to be associated with the severity of COVID-19. the anti-IL-6 and other cytokine/chemokine-related elements are potential block targets for the management of COVID-19 cytokine secretion syndrome. there is interest in using selective nAb transmission as a treatment. identifying nAbs produced during natural infections such as patients recovering from SARS-CoV-2 infection or SARS-CoV-1 due to the similarities between SARS-CoV-1 and 2 or through animal vaccination methods are important. transferring plasma (CP) from people previously infected with SARS-CoV-2 have evaluated the safety and potential efficacy of plasma therapy in patients with severe disease. However, there is no specific treatment for COVID-19 disease but there are candidates with positive effect. Some candidates prevent the virus entry into the host cell while some other candidates prevent the proliferation of it and etcetera. So it is important to identify virus pathogenesis and also treatment candidates.

Conclusion: In this study, the mechanism of virus pathogenesis and effective drugs in blocking each stage of virus spread were investigated due to the necessity of Choosing the right medicine for people with Covid-19.

Keywords: SARS-CoV-2,COVID-19,treatment

COVID-19 treatments | A glance at the most recent reported drugs, which may close to the operational phase. (Review)

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Introduction: Due to the increasing spread of the Coronavirus, 2019 (COVID-19), the competition for the most successful possible solution has become very popular among different countries. Therefore, addressing the issue of which is the next most likely candidate to enter the global market; It is a question that sooner or later every country must answer.

Methods: This study planned based on the latest published information on drugs that are currently undergoing the fourth clinical phase of the estuary, has tried to cover the common concern, which means that recent reports indicate the importance of which of the existing or newly synthesized drugs in the control of this disease? In this review, extensive investigations in PubMed, Scopus, and Google Scholar have been performed using keywords including Budesonide, Lenalidomide, Linagliptin, Acetylcysteine, and Gamolenic acid Accordingly, the most important research papers about this subject based on the quality and level of pieces of evidence have been collected, categorized, and discussed.

Results: The findings suggest that the introduced chemical structures are evidence of measurable success on a laboratory scale, but there are no reliable reports of the high potency of these drugs to control or treat COVID-19 in the long term. It is clear that much of the existing treatment methods have resulted out from an understanding of the previous 2 outbreaks, particularly the SARS-CoV outbreak which shares similarities with the novel strain of the Coronavirus. However, to generate treatments with high efficacy, the unique features of SARS-CoV-2 must be understood to a greater extent, especially its spike protein. Besides these, different serotypes are being identified in different countries with a slight variation which may respond to a different host response, pathogenesis, and symptoms in different regions.

Conclusion: In conclusion, FDA approved most of these drugs permanently or under a specific condition, it is obvious that scientists had to get along with trial and error these days to overcome the probable upcoming catastrophe.

Keywords: Coronavirus, COVID-19, Treatments, Laboratory experiments, Trial and error, FDA.

Creation of the first patient information database in pelvic floor department (Research Paper)

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Introduction: Pelvic floor dysfunction is usually associated with impaired normal function and can includes range from a variety of conditions such as urinary incontinence (SUI), fecal incontinence, pelvic organ prolapse, lower urinary tract abnormalities, and fecal discharge. Pelvic floor dysfunction poses clinical challenges and increasing financial pressure in national health care. On the other hand, Electronic Medical Record (EMR) system is one of the most important items in the hospital information system and an essential technology to improve the quality of care. Therefore, it was decided to launch the electronic registration of patient information as a project.

Methods: To create an electronic record, after Preparation Proposals and design process the following steps were taken: Coordinate with a skilled person in the design of medical electronic records, Select the items required to be registered in the patient file, Dividing the items into two essential and optional section, Trial use of the prepared e-file and solving possible problems and Providing the necessary facilities for full use for all patient.

Results: By entering the information of each patient, the designed system provides a history report that is text-based;also all information is available in Excel format for research purposes

Conclusion: To improve the quality of care and patient satisfaction, it was decided to launch the electronic registration of patient information as a project. We design a special patient information record software for pelvic floor clinic and we hope this EMR can help us to better education , better research and better healthcare

Keywords: pelvic floor, electronic medical record, medical data

Criminal Law in Protection of Bioethics, Against The Negligent Outbreak of COVID-19 (Review)

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Introduction: The spread of the Coronavirus worldwide has transformed all areas of human life and even led to the evolution of theories and approaches in the humanities, including bioethics and legal sciences. Civil law, labor law, criminal law, human rights, and many other fields of law have evolved from the COVID-Pandemic. One of the legal norms governing human relations is the legal response to damage to health and loss of life and legal prevention of these behaviors. Pervasive crises with inhuman causes are becoming more prevalent with human carelessness. One of the legal norms governing human relations is the legal response to damage to health and loss of life and legal prevention of these behaviors. Pervasive crises with inhuman causes are becoming more prevalent with human carelessness. Violation of the right to life and human health, as the most fundamental human right, is analyzed in the knowledge of bioethics, and among the legal sciences, criminal law has the greatest interest in protecting these two rights. Criminalization, trial, punishment, and criminal prevention are ways in which criminal law protects bioethics in the face of neglect of life as a moral and human value.

Methods: This article analyzes the patterns of legal and criminal protection of bioethics in a descriptive-analytical manner - which is common in humanities research, especially in law. In particular, the method of "discourse analysis" of the shortcomings of Iran's criminal law, and especially the provisions of the Islamic Penal Code on murder due to indifference and negligence to the moral value of life and health of others - in determining whether the negligence in adhering to health protocols that leads to more spread of Corona-virus is criminal or not.

Results: In the prevalence of pandemics, especially COVID-19, Iranian criminal law lacks the necessary classifications to accurately determine the title of responsibility - and consequently the application of crimes and the exercise of appropriate criminal responsibility - in pandemic crimes; and this shows the immorality of Iranian law regarding the punishment of murder due to the culpable transmission of a the deadly virus. Iran's criminal law needs to be amended and new legislation to adequately cover the system of criminalization. Most of these crimes include: misdiagnosis of the disease (if it affects the patient's deterioration), production and distribution of defective diagnostic and therapeutic equipment and prescriptions, failure to provide information at various levels depending on the job, and crimes due to Violation of quarantine regulations.

Conclusion: Iran's criminal law needs to be amended and new legislation to provide adequate coverage of the criminal prosecution system following the spread of epidemics.

Keywords: Bioethics, criminal law and ethics, unintentional transmission of the virus

CRISPR Cas13: a potential therapeutic option of COVID-19 (Review)

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Introduction: The novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can be considered as the most important current global issue, as it has caused the novel coronavirus disease (COVID-19) pandemic, which has resulted in high mortality and morbidity rates all around the world. Although scientists are trying to discover novel therapies and develop and evaluate various previous treatments, at the time of writing this paper, there was no definite therapy and vaccine for COVID-19. So, as COVID-19 has called ideas for treatment, controlling, and diagnosis, we decided to present our hypothesis, which has received less attention, about treating COVID-19 through CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) Cas13.

Methods: searching online on google scholar, PubMed, and Scopus based on the keywords including COVID-19, CRISPR Cas13, SARS-CoV-2, genome, and treatment.

Results: COVID-19 outbreak, accompanying numerous of pneumonia cases caused by SARS-CoV-2, emerged in Wuhan, a city in the Hubei province of China, late 2019. Although it was indicated that the patients infected with SARS-CoV-2 (formerly named 2019-nCoV) in China might have used (as a source of food) or encountered infected animals in the seafood market, more inquiry displayed some patients with no record of visiting the seafood market. So, the person-to-person contagion of the virus through coughing, sneezing, aerosols that could infiltrate to lungs via nose or mouth is inevitable. There are seven coronaviruses that caused disease in humans. Two strains with zoonotic origination containing Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) were connected to the emergence of severe respiratory diseases in humans in 2003 and 2012 subsequently, and now, SARS-COV-2 as the seventh virus of the coronavirus family has caused severe respiratory diseases pandemic in humans. As it is severely contagious, there is a rapid progression in morbidity and mortality rates of COVID-19, and there is no certain vaccine and treatment for that, the best solution for controlling the pandemic in addition to following preventive methods can be suggesting and finding probable effective therapies. In this paper, we have suggested CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) Cas13 as a potential therapy, in various aspects, of COVID-19. Clinical manifestations Clinical manifestations are variable based on various reasons. Although the primary symptoms of COVID-19 are prevalently identified as cough, fever, shortness of breath, in another investigation, confusion, chest pain, nausea, and vomiting were the most prominent COVID-19 symptoms and coma was reported in one study. Not only the American Academy of Otolaryngology has reported the loss of sense of smell and taste disorder (anosmia and dyspepsia) in some COVID-19 patients, but also they were even the unique signs in some of them. It must be noticed that viral conjunctivitis must be regarded as a probable early manifestation of COVID-19. Besides, SARS-CoV-2 can cause

acute kidney failure and involve the cardiovascular system and the Gastrointestinal system. 2019-nCoV features Although the viral genome analysis revealed that SARS-CoV-2 (formerly named 2019-nCoV) is 88% similar to bat-SL-CoVZC45, bat-SL-CoVZXC21 and 96.2% identical to a bat CoV RaTG13, recent studies proposed Malaysian smuggled pangolins to China, along with some probable alternative intermediate hosts like turtles and snacks as the probabilistic provenance of the virus. Moreover, the most genomic encoded proteins of SARS-CoV-2 are 79.5% and 51% identical to SARS-CoV and MERS-CoV respectively, and resembling SARS-CoV it uses ACE2 receptor for cellular entry which the high virus affinity to the ACE2 receptor is perhaps due to natural selection rather than premeditated manipulation. Coronavirus spike (S) protein has been ascertained as a substantial determinative of virus entry into host cells as the receptor-binding domain (RBD) for binding to ACE2 receptor, and direct membrane fusion between the virus and plasma membrane has been placed on the head of that. Furthermore, alongside the membrane fusion, the clathrin-dependent and -independent endocytosis mediates the SARS-CoV entry. After admittance, the viral RNA genome is liberated into the cytoplasm and is translated into two polyproteins and structural proteins, after which the viral genome begins replication. The newly formed envelope glycoproteins are intromitted into the membrane of the endoplasmic reticulum or Golgi, and the nucleocapsid is composed via compounding the genomic RNA and nucleocapsid protein. Afterward, viral particles bud into the endoplasmic reticulum-Golgi mediator compartment (ERGIC). Eventually, for releasing the virus out of the infected cell, the vesicles containing the virus particles fuse to the plasma membrane. Novel coronavirus or 2019-nCoV is an enveloped, positive-sense, and single-stranded RNA beta-coronavirus, which is about 29.9 kb with a cap structure at its 5′ end and a poly-A tail at the 3′ end. Like other coronaviruses, it has particular viral replicase genes in a variable number (6–14) open reading frame (ORF), which codifies vital proteins (27-29 ones) for viral replication, nucleocapsid, and spikes formation. Two-thirds of viral RNA, principally placed in the 5′-terminal in the first ORF (ORF1a/b) translates two polyproteins, pp1a and pp1b, which codifies 16 non-structural proteins (NSP), whereas the rest of ORFs encode at least 8 accessory proteins (ORF3a, ORF6, ORF7a, ORF7b, ORF8, ORF9a, ORF9b, and ORF10) intervening with the host innate immune response. It must be mentioned that there are intra-viral protein-protein intercommunications between most of these proteins, which make the situation more complicated than before.

Conclusion: In conclusion, among various potential therapeutic options of COVID-19, CRISPR Cas13 has been omitted. However, it has the potential to be successful against SARS-CoV-2.

Keywords: CRISPR Cas13, SARS-CoV-2, genome, and treatment.

CRISPR/Cas-based detection of COVID-19 (Review)

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Introduction: The new coronavirus 2019 (COVID-19), which has affected millions of people all over the world has caused very great worldwide concern. The COVID-19 outbreak began in Wuhan, China and has spread rapidly all over the world, leading to the death of many people, and the number of cases of disease and mortality is increasing by the day. COVID-19 pandemic disease is caused by SARS-CoV-2 which is closely related to SARS-CoV [1]. This class of viruses is enveloped and has an RNA genome in size of almost 26-32 kb. SARS-CoV-2 contains 4 structural proteins called Spike (S), Nucleocapsid (N), Membrane (M) and Envelope (E) proteins which enter the host cell via S protein and replicate its own genome within the host cells [2, 3]. One of the major causes for the widely and rapid spread of the COVID-19 disease is the presence of a large number of asymptomatic COVID-19 positive cases. Therefore, the development of efficient diagnostic methods for sensitive, rapid and accurate diagnosis is essential for early diagnosis of this disease. The standard molecular technique for detecting SARS-CoV-2 worldwide is currently RT-qPCR. However, this technique faces challenges such as limited access to the required reagents, the need for trained personnel, need for equipped laboratories, and the long time required to achieve the final result. Precision, speed, efficiency, simplicity, and a broad range of CRISPR (clustered regularly interspaced short palindromic repeats) systems applications have motivated researchers to develop rapid and sensitive SARS-CoV-2 diagnostic systems based on CRISPR. Results of various studies on the use of the CRISPR system in the detection of SARS-CoV-2, have shown that CRISPR-based diagnostic systems for the diagnosis of SARS-CoV-2 have benefits such as high diagnostic speed, even in 30 min, no need for a well-equipped laboratory, portability, as well as high sensitivity and accuracy [4-6].

Methods: In writing this review article, we searched in various databases such as google scholar for keywords related to CRISPR and COVID-19 detection, and selected the most suitable papers.

Results: Since the outbreak of COVID-19, different groups have been working on CRISPR-based diagnostic systems for rapid and sensitive diagnosis of SARS-CoV-

2. For instance, Ding et al. could successfully detect SARS-CoV-2 in 40 minutes, by developing the All-In-One Dual CRISPR-Cas12a (AIOD-CRISPR) system. AIOD-CRISPR system has advantages such as high sensitivity, high precision, high speed, single-molecule sensitivity and the capacity to naked-eye observe test results [7]. While the development of CRISPR-based diagnostic systems for the rapid detection of SARS-CoV-2 nucleic acid has been given special attention, these platforms have not addressed mutations and genomic editions relevant to the nucleic acid of the virus. In this regard the VaNGuard (Variant Nucleotide Guard) method was developed in an attempt to rapidly and sensitively identifying as well as recognize mutated and altered regions of the SARS-Cov-2 genome. The powerful, sensitive and fast VaNGuard system was found to be able to detect SARS-CoV-2 in 30 minutes [8]. A simple chemical method called STOP (SHERLOCK Testing in One Pot) was established in another try, capable of detecting COVID-19 in an hour. The STOP system is comparable in terms of sensitivity to RT-qPCR-based methods and has benefits such as simplicity, suitable for point-of - care, sensitivity, low cost, availability of test components and no need for RNA extraction [9].

Conclusion: Due to the advantages of CRISPR-based diagnostic systems such as high speed, simplicity, portability, high sensitivity and high specificity in the diagnosis of SARS-CoV-2, these diagnostic systems can be widely used to manage COVID-19 and future pandemics

Keywords: COVID-19, SARS-CoV-2, CRISPR

Cytotoxic activity of doxorubicin in combination with methanolic extract of Crocus pallasii subsp. (Research Paper)

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Introduction: Doxorubicin is a chemotherapeutic agent that is used in the treatment of cancers, but its clinical application is limited due to serious side effects such as cardiotoxicity. Methanolic extract of Crocus pallasii subsp. haussknechtii corms exhibits cytotoxicity effects on MDA-MB-231 human breast cancer cell line at the concentrations higher than 100 µg/mL. In this study, cytotoxic effects of doxorubicin alone and in combination with methanolic extract of Crocus pallasii subsp. haussknechtii corms on MDA-MB-231 tumor cell line were investigated.

Methods: Stock solution of methanolic extract was prepared in dimethyl sulfoxide (DMSO), and serial dilutions were prepared in phosphate-buffered saline (PBS). The final concentration of DMSO in all experiments was 1%. Different concentrations of doxorubicin and corms extract were added to the cultured cells and incubated for 48 h. Cell survival was evaluated using the cell viability MTT test. All data were analyzed by SPSS software version 20.0 and mean comparison of data was performed based on Duncan test at $P < 0.05$ level.

Results: The results indicated that the methanolic extract of Crocus pallasii subsp. haussknechtii corms at the concentrations less than 100 µg/mL did not reduce cell viability and has a growth inhibitory effect at the higher concentrations. Doxorubicin alone at all the tested concentrations (0.46, 0.92, 4.6, and 9.2 nM) induced cell growth inhibition in MDA-MB-231 cells, with IC50 values of 3.05±0.04 nM at 48 h. Co-treatment of doxorubicin and the corms extract at 25 and 50 µg/mL concentrations reduced the percentage of cell viability in a dose-dependent manner. The IC50 value of doxorubicin in the presence of the corms extract against MDA-MB-231 cancer cells was less than 0.46 nM at 48 h.

Conclusion: Methanolic extract of Crocus pallasii subsp. haussknechtii corms potentiates doxorubicin cytotoxicity against MDA-MB-231 breast cancer cells. Thus, co-administration of doxorubicin and the corms extract of Crocus pallasii subsp. haussknechtii as a medicinal plant may be a useful strategy for enhancing the chemotherapeutic effects of doxorubicin at lower concentrations.

Keywords: Breast cancer; Anticancer; Crocus pallasii; Doxorubicin

Design and synthesis of chitosan nanoparticles conjugated with folic acid for targeted transfer of miR-126 to lung cancer cell lines (Research Paper)

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Introduction: Introduction: Lung cancer is still the most common cancer globally. Early screening remains the key to improve the prognosis of patients in recent years, studies have found that miRNAs play an important role in lung cancer. MicroRNA-126 is a tumor suppressor microRNA which is significantly down regulated in lung cancer cell lines, such as A549 cells and has been reported to be used as a therapeutic target for lung cancer. However, the delivery of miRNA has always been limited by many barriers. In the present study, miR126 loaded gene delivery system based on chitosan nanoparticles conjugated folic acid was prepared in order to deliver cs-FA-miR126 into A549 cells

Methods: Materials and methods: The nanoparticles were characterized using dynamic light scattering(DLS), Fourier transform infrared spectroscopy (FTIR) and transmission electron microscopy (TEM). The manner of miRNA loading was speculated by gel retardation assay. Dose dependent cellular toxicity by Cs-FA-mir126 and Cs-FA-miR scramble was demonstrated by MTT. The expression of key genes in apoptosis (BAX, caspase 9) and autophagy (Becline1, ATG5) process were assumed by Quantitative Real Time PCR. The function of nanoparticles in the Apoptosis and cell cycle arresting were evaluated by flow cytometery. Moreover, in vitro nanoparticle efficacy on metastasis inhibiting was evaluated through scratch test.

Results: Results : Nanoparticles were produced based on modified ionic gelation of tripolyphosphate(TPP). DLS confirmed small sized nanoparticles (<200). while FTIR confirmed different functional groups associated with synthesized nanoparticles.MTT analysis results showed that cell viability in cs-FA-mir 126 treatmentation group was significantly lower than that control groups.the result showed that cs-FA-miR126 group overexpression inhibits the A549 cell viability. Flowcytometry results demonstrated that the number of apoptosis cells in cs-FA-miR126 treatmentation groups was significantly higher than that the cs-FA-miR scramble and control groups. the expression of EGFL7 was reduced and the expression of BAX, caspase9, ATG5, Beclin1 were increase remarkably. Cs-FA-miR126 can induce apoptosis of the A549 cells by regulatory the expression of BAX, caspase 9, ATG5, Beclin1.

Conclusion: In conclusion, our study suggest that folic acid conjugated chitosan nanoparticles can mediate the delivery of Mir-126 directly into lung tumor cells while preserving its molecular and biological activity.

Keywords: Key words: Chitosan nanoparticle, miRNA-126, Folic acid, Apoptosis, Autophagy.

Design and synthesis of folic acid conjugated chitosan-PEG nanoparticles for targeted drug delivery of sodium butyrate to prostate cancer cells (Research Paper)

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Introduction: Prostate cancer is the sixth most common cancer in the world and the second most common cancer in men. Sodium butyrate, a histone deacetylase inhibitor, is a promising anticancer drug for many cancers. Our aim is to make folate-targeted chitosan nanoparticles containing sodium butyrate for the treatment of prostate cancer named CS-PEG-FA-SB.

Methods: In addition to the physical properties of the final nanoparticles by DLS, FTIR, TEM and SEM techniques, the toxicity of the final nanoparticles at different concentrations of the drug will be evaluated by MTT method. Furthermore, the expression of genes involved in autophagy and apoptosis in prostate cancer cell lines (PC3 and DU145) and comparison with Folate receptor negative cell line (PC3) and normal cell line (HFF-1). After treatment with chitosan nanoparticles targeted with folic acid and containing chemotherapeutic drug sodium butyrate, the apoptotic and autophagy genes were assessed by Quantitative Real time PCR method. The functional analysis of nanoparticles was examined by Apoptosis and cell cycle arrest flowcytometery analysis. Finally, the results will be evaluated with SPSS software and t-test and one-way ANOVA.

Results: Cells treated with folic acid-targeted chitosan nanoparticles containing sodium butyrate chemotherapy showed significant and dose-dependent differences at different times. The lethality of this drug nano system in PC3, DU145 and HFF-1 cells was demonstrated using MTT assay. The results of morphological study showed that chitosan nanoparticles targeted with folic acid and containing sodium butyrate chemotherapy (CS-PEG-FA-SB) have a suitable size 100±20 nm with spherical appearance. The Real Time PCR analysis showed the significant expression of apoptotic and autophagy genes in DU145 cell line treated by CS-PEG-FA-SB. The apoptosis and cell cycle arrest analysis confirmed the significant effect of CS-PEG-FA-SB treated DU145 cell line in compare with treated PC3 and HFF_1 cell lines.

Conclusion: Folic acid-targeted chitosan nanoparticles containing sodium butyrate chemotherapy drug can inhibit growth in DU145 cell line in compare with PC3 and HFF-1 cell lines, which may induce cell death by increasing the expression of apoptotic and autophagic genes. These findings could open up effective insights into prostate cancer treatment strategies.

Keywords: Prostate cancer, Apoptosis, Autophagy, Chitosan nanoparticles, Sodium butyrate, Folic acid

Design and synthesize of Folic Acid conjugated MOF-Chitosan nanoparticles containing LNA miRNA-224 antisense for targeted gene therapy of Colon Cancer (Research Paper)

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Introduction: With the ability to control the expression of genes, miRNAs can be considered as one of the regulators of biological processes. Nanoparticles also have the ability to cause many factors at their level, including drugs, fluorescent dyes, and various ligands. Conjugate that all of these factors are effective in prolonging their survival in the blood and increasing the correct targeting of tumors . in this study, targeted MOF-Chitosan nanoparticles were synthesized with folic acid-containing miRNA-224 antibody sequence and were used to inhibit folic acid-receiving clone cancer cells. Thus, processes related to inhibiting cancer processes such as growth inhibition, cell death, apoptosis, and autophagy were examined in cellular and molecular forms

Methods: In this project, MOF nanoparticles of zinc acetate nanoparticles were first synthesized in dimensions of less than 200 nm and the quality of synthesis was evaluated by DLS, FTIR, and TEM methods. In addition, cell toxicity, apoptosis, and cell cycle inhibition were assessed by cellular and molecular methods such as MTT, Real-time PCR, Cell cycle arrest Flowcytometry, Flow cytometry annexin V. In this project, MOF nanoparticles were synthesized with chitosan coating and then conjugated with folic acid.

Results: TEM results show spherical morphology with the porous center and jelly margin of chitosan-folic acid, FTIR results prove the connection of covalent folic acid and chitosan and the creation of MOF networks. Cellular analyzes of these nanoparticles show the targeted toxicity of MCFM224 nanoparticles to HCT116 cancer cells. The cell death type was confirmed by apoptosis and cell cycle control tests. The molecular analyzes of the treated cells show high expression of BAX and Caspase 9 apoptosis genes and Beclin1 and mTORC1 autophagy genes, which indicate the induction of delayed and autophagic apoptosis in HCT116 cells. The cell death type was confirmed by apoptosis and cell cycle control tests. The molecular analyzes of the treated cells show high expression of BAX and Caspase 9 apoptosis genes and Beclin1 and mTORC1 autophagy genes, which indicate the induction of delayed autophagic and apoptosis in HCT116 cells. The toxicity of nanoparticles and the viability of cells were assessed by the MTT test, which indicated high mortality of MCFM224 nanoparticles in the HCT116 cell lines. Since HCT116 cells represent folic acid receptors, they showed significant mortality

compared to normal CRL1831 intestinal cells, with molecular and cellular results confirming this. The results of flow cytometry of apoptosis performed using annexin v and pi indicate a high percentage of apoptosis in HCT116 cells treated with MCFM224 nanoparticles. In addition, the inhibition of the cell cycle confirms the cellulosic apoptosis of cells that were treated at the same time and at the same concentration and under the same conditions. An increase in the percentage of cells in the Sub-G1 phase indicates the induction of apoptosis and the planned death of treated cells.

Conclusion: According to the results of various studies in recent years, as well as the research conducted in this study, we can hope to treat cancer with the help of MOF-Chitosan nanoparticles and also combine it with microRNA antisense strand, which by conducting research and Further studies can achieve better results in the treatment of colon cancer.

Keywords: colorectal cancer, MiRNA224, LNA, gene therapy, nanoparticles

Designing a novel vaccine candidate for breast cancer (Research Paper)

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Introduction: The most prevalent cancer in women over the world is breast cancer. Immunotherapy is a promising method to effectively treat cancer patients. Among various immunotherapy methods, tumor antigens stimulate the immune system to eradicate cancer cells. Preferentially expressed antigen in melanoma (PRAME) is mainly overexpressed in breast cancer cells and has no expression in normal tissues. FliCΔD2D3, as truncated flagellin (FliC), is an effective toll-like receptor 5 (TLR5) agonist with lower inflammatory responses. The objective of the present study was to utilize bioinformatics methods to design a chimeric protein against breast cancer.

Methods: The physicochemical properties, solubility, and secondary structures of PRAME+FliCΔD2D3 were predicted using the tools ProtParam, Protein-sol, and GOR IV, respectively. The 3D structure of the chimeric protein was built using I-TASSER and refined with GalaxyRefine, RAMPAGE, and PROCHECK. ANTIGENpro and VaxiJen were used to evaluate protein antigenicity, and allergenicity was checked using AlgPred and Allergen FP. Major histocompatibility complex (MHC) and cytotoxic T-lymphocytes (CTL) binding peptides were predicted using HLApred and CTLpred. Finally, B-cell continuous and discontinuous epitopes were predicted using ABCpred and ElliPro, respectively.

Results: The stability and solubility of PRAME+FliCΔD2D3 were analyzed and its secondary and tertiary structures were predicted. The results showed that the derived peptides could bind to MHCs and CTLs. The designed chimeric protein possessed both linear and conformational epitopes with a high binding affinity to B-cell epitopes.

Conclusion: PRAME+FliCΔD2D3 is a stable and soluble chimeric protein that can stimulate humoral and cellular immunity. The obtained results can be utilized for the development of an experimental vaccine against breast cancer.

Keywords: PRAME antigen, Vaccines, Breast cancer, Bioinformatics

Detection of novel Coronavirus by CRISPR/Cas technology (Review)

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Introduction: The first and foremost step to overcome SARS-CoV-2 is to identify infected people in that detection can cut off the virus transmission cycle. There are different kinds of detection methods, such as quantitative PCR assay, antibody and antigen-based detection methods, and CRISPR-based tests, which have their advantages and disadvantages.

Methods: We gather information by searching key words of SARS-CoV2 , COVID19, diagnostic tests and CRISPR/Cas in Google scholar.

Results: Soon after SARS-CoV-2 emerged in Wuhan, the capital of Hubei province in China, both DETECTR and SHERLOCK developed to identify NA of this virus more accessible and timesaving. To be more precise, the total workflow of CRISPR/Cas12a is approximately 30 minutes, and its LOD is 70-300 copies/µL input. On the other hand, SHERLOCK based detection spends more time (less than one hour), and its LOD is 10-100 copies/µL input .Recently, in May 2020, Sherlock Biosciences (Cambridge, USA) received the first FDA-approval for the Sherlock SARS-CoV-2 kit. A wide range of specimens can be used in this kit, such as a nasal swab, oropharyngeal swab, BAL, and nasopharyngeal swabs.

Conclusion: There is imperative potential in the use of CRISPR-based detection assays to fulfill the need for more rapid, more precise, and affordable methods, making it foregone technology to use in the future. However, we need to carry out more research on the evaluation of these new approaches.

Keywords: Coronavirus, SARS-CoV-2, COVID19, Diagnostic tests, CRISPR/Cas

Determination of Novel miRNA-target Interactions in Endometrial Cancer Using Network Analysis (Research Paper)

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Introduction: Endometrial cancer (EC) is considered as one of the most common cancer in women with 380,000 new cases wordwide every year. In addirion, EC is known as a disease which mainly affects postmenopausal women (more than 90% with the age above 50 years). The current classification of endometrioid adenocarcinoma is only based on the histology which directs subsequent therapeutic management. However, the approach is often insufficient for prognosis. Therefore, new approaches should be developed to identify and characterize novel biomarkers for understanding different subtypes better, improving prognosis assessment, and optimizing patient care. MicroRNAs are particularly attractive candidates as biomarkers.

Methods: Microarray data in Gene Expression Omnibus (GEO) was used to obtain the EC-involved miRNA. Then, MiRSystem, as an integrated system for predicting target mRNAs and their associated pathway, was applied to find significant pathways. Subsequently, the genes of these pathway were selected and the miRNAs regulating these genes were determined. Further, Venn diagram was utilized to calculate the intersection of the list of elements. Finally, miRNA-target interactions were visualized by Cytoscape.

Results: the findings revealed that four miRNAs ("miR-103a-3p", "miR-107", "miR-424-5p", and "miR-497-5p") involved in the mitogen-activated protein kinases (MAPK) signal pathways. Moreover, according to the result of the Venn diagram represented the association between three genes (RPS6KA3, NTRK2, MAP3K3) with the miRNAs.

Conclusion: Based on the results, the miR analysis of endometrial tumor tissue complements the classical anatomo-pathological approach and adds prognostic and therapeutic value.

Keywords: Biomarker, Endometrial cancer, In silico analysis, miRNAs

Developing an interface to simply check protein mutations for protein engineering (Research Paper)

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Introduction: Protein engineering is a widespread approach in the branch of structural biology. It is useful to redesign proteins to improve its function; correct incorrect protein folding or increase protein resistance about some environmental factors such as temperature. The first problem in protein engineering pipeline is what residue/s should be mutated and what residues should be replaced. We can use bioinformatics tools to decrease the problem space. OSPREY is one of this software that can be used to check different mutations and check protein energy and choose best mutations to check them in molecular dynamic tools such as Gromacs. OSPREY time complexity is very lower than molecular dynamic programs and its results are reliable but it's not user friendly and usage of it be difficult for biologists. We develop a user-friendly interface for OSPREY to check different mutations. This interface works in protein and protein-peptide mode. It can help biologists to check difference mutations without conflict with program complexity.

Methods: Our interface input file is a PDB file. We alert users to add hydrogens to the protein files before check mutations. Users write protein chain name and residue number and write some amino acids to replace. Users write these details for any residue number in one line. In protein-peptide mode, the user should define the beginning and end of protein and peptide sequences and write mutations such as protein mode. The software results will display in .text format and it includes mutations and their energies. This software developed with PHP language.

Results: This interface helps biologists to simply check different mutations on proteins or protein-peptide complexes and select the best mutations according to energies.

Conclusion: The usage of bioinformatics tools is very important in experimental problems such as protein engineering. It decrease the time and cost complexity of the problem but these tools usage is difficult for biologists. we develop an interface for OSPREY software to check different mutations without conflict with software complexities.

Keywords: protein, protein engineering, mutation, peptide design, protein- peptide interaction

Diagnosis of Hereditary tyrosinemia type 1 (Review)

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Introduction: Tyrosinemia type 1 (HT1) also known as fumarylacetoacetase deficiency (EC: 3.7.1.2), is a rare inherited autosomal recessive disease that results from a disturbance in the metabolism of an amino acid. The disease is caused by defective activity of the enzyme fumarylacetoacetate hydrolase (FAH), which catalyzes the final stage of tyrosine catabolism; Leads to the accumulation of toxic metabolites. Early diagnosis is essential because early medical management, which includes restricting the diet rich in phenylalanine and tyrosine, prevents the accumulation of toxic metabolites, and prevents the development of chronic liver disease, tubular kidney damage, and liver cancer. Symptoms occur at different times depending on the type of disease. It may occur in the acute form of the disease during the first few months, in the semi-acute form in the second half of the first year, or in the chronic form in later years to adulthood.

Methods: We conducted searches in the following electronic databases: Pubmed, Embase, Web of Science, and google scholar. We searched using text word and MeSH terms relating to “Tyrosinemia type 1 OR inborn errors of metabolism”, AND “succinylacetone OR DBS”. The search was conducted on 26th January 2019 without any restriction in time and language. We examined reference lists of included studies and previous reviews.

Results: Although there are many causes of tyrosinemia, hereditary tyrosinemia can be diagnosed from clinical symptoms and biochemical analysis. Diagnosis of tyrosinemia type I would be based on examination of urinary organic acids. The level of succinylacetone in the serum of infected people is excreted in the urine, which is the basis for the diagnosis of hereditary tyrosinemia type I. Excretion of succinyl acetone in the urine causes the urine to smell like cooked cabbage or rotten mushrooms. Other way to diagnosis is plasma amino acids measurement which detected by high/or normal tyrosine level and increased methionine. In addition, Urine porphyrins is other diagnosis method. Delta aminolevulinic acid (due to inhibition of delta aminolevulinic hydrate by enzyme succinyl acetone) was increased in the patients. The best method to detect tyrosinemia is measuring of Succinylaceton (SA) in blood and urine. Succinyl acetone enters the mitochondria of renal lymph nodes and inhibits the Krebs cycle of aminolevulinic acid hydrate (which is also a precursor to synthesis) and increases tubular damage.Screening for tyrosinemia type1 using burst mass spectrometry measurements of SA from dry bloodstains seems promising. NBS using MS/MS detection of SA in bloodstains is the best current method for early detection of HT-1. After a positive NBS result, it is best to repeat the SA test with a new urine sample as soon as possible; Also perform tests such as liver function tests (PT, aPTT, aspartate transaminase or alanine transaminase), AFP, PAA, electrolyte and glucose. If HT-1 is highly suspected, plasma amino acids (PAA) and liver function tests such as prothrombin

time (PT),(INR), partial thromboplastin time (PTT), and α-fetoprotein(AFP) should be evaluated at the first examination. Nowadays, molecular tests is one of the best method to diagnose genetic disorders. Analysis of FAH gene mutation is one of the best choice for patients. More than 100 mutations in the gene encoding fumaryl acetate hydrolase (FAH) cause type 1 hereditary tyrosinemia (HT-1). Some known mutations reduce the catalytic activity of FAH. The use of blood SA as an NBS marker is expected to detect all infants with HT-1. Most of these babies with HT-1 can live a life without liver or kidney disease if they are properly diagnosed and medically treated. After confirmation of the diagnosis, NTBC and diet treatment should be started immediately.

Conclusion: Tyrosinemia type 1 is an autosomal recessive disease; diagnosis of this disease can be done before or after birth by genetic testing and amniotic fluid testing, neonatal screening tests, plasma SA levels, plasma amino acid levels and liver tests. Early diagnosis with medical management can reduce the symptoms and complications of the disease. Readily available diagnostic tests are too insensitive to distinguish between these variants, and more definitive but technically difficult tests can be performed rapidly in only a few centers. Therefore, effective management may be compromised, due to the inability of obtaining a working diagnosis quickly.

Keywords: Tyrosinemia; inborn errors; Diagnosis; Newborn screening

Diet before puberty and its effects on puberty and after (Systematic review((Review)

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Introduction: Nutrition plays a direct and key role in creating, maintaining and promoting health because nutrition is necessary for all vital functions of the body. Proper nutrition is one of the most important issues related to puberty. And this largely depends on proper nutrition before puberty, so that sometimes the diseases of puberty, such as obesity, lack of proper height growth, etc., are rooted in improper nutrition before puberty. Studies have shown that malnutrition habits occur before puberty and, as a result, during puberty.

Methods: This review is published in articles on databases Pubmed, sid , google scholar, Magiran From 2010 to 2020 .A search of the databases turned up 146 articles, 73 of which were not relevant to the research, were removed by reading the abstract, and finally 32 studies were selected. It was done in Persian and English

Results: Finally, 18 articles were included in this study. Some studies have shown that the incidence of developmental disorders and diseases related to puberty is directly and significantly related to diet before puberty. When the adolescent body needs nutrients for development and growth, but there is a limit to the quality and quantity of the diet and this need is met with non-nutritious foods, it provides the basis for developmental disorders and disease during puberty. Therefore, it can be said that the quantity and quality of nutrition before puberty is very important on the developmental stages of puberty.

Conclusion: The results of the present study show that in general, the type and amount of diet has a direct effect on the age of onset of puberty, growth rate, disorders and diseases during puberty. Therefore, caring for and improving the quality and quantity of children's nutrition guarantees proper growing and health that during puberty and adulthood that it preserves and promotes the health of the next generation.

Keywords: Effect ,Diet, Before, puberty,after

Differences in maturation and quality of oocytes/follicles with polycystic ovarian syndrome following freezing-thawing (Research Paper)

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Introduction: Background and purpose: One of the current methods during assisted reproductive techniques is cryopreservation, specially freezing of oocytes/follicles. During this process, the genes involved in apoptosis may change and can effect on the quality of the frozen oocytes/follicles. There is still no information on the difference in in-vitro maturation potential and quality of PCOs follicles/oocytes (such as apoptosis rate) following freezing-thawing process compared to normal oocytes/follicles, which has been studied in this study. The expression of BAX and BCL2 genes was investigated as apoptosis genes in normal and PCOs oocytes/follicles following freezing-thawing.

Methods: Materials and methods: 10 NMRI mice were divided into two groups: control and PCOs groups. The PCOs mice were induced by intramuscular injection of 4 mg/kg estradiol valerate dissolved in 0.2 mg Sesame oil once a day. After 60 days, mice of each group were sacrificed and their ovarian tissue was collected. After separating the oocytes/follicles, the freeze process was done. Then, thawed oocytes and follicles were cultured in IVM medium (MEM-alpha culture medium with 10% FBS serum), and incubated for 24 to 48 hours. The oocytes/follicles were examined to express the BAX and BCL2 genes using Real Time-qPCR method.

Results: Results: The results showed that 58% of oocytes and 50% of follicles were matured in the PCOs group following freeze-thaw method. In addition, 65% of oocytes and 88% of follicles were matured in the normal freezed-thawed group. The rate of in-vitro oocyte maturation in the normal freezed-thawed group was higher than the PCOs freezed-thawed group ($P< 0.05$). Also, the apoptosis rate was also increased in PCOs freezed-thawed group compared to control group ($P< 0.05$).

Conclusion: Conclusion: PCOs oocyte/follicle quality was decreased after freeze-thaw process. The maturation and survival rate of PCOs oocytes was also changed during cryopreservation that it states that the freezing process is not recommended for these oocytes/follicles.

Keywords: Keywords: IVM, Vitrification, Polycystic ovarian syndrome, Cryopreservation, Oocyte, BAX, BCL2.

Direct Oral Anticoagulants therapy in Iran (Review)

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Introduction: Thrombosis and bleeding are two sides of the double-edged sword of hemostasis. Bleeding disorders are associated with a high rate of morbidity and mortality. Management of thrombosis and bleeding has improved significantly in recent years. Advancements in recombinant coagulation factors synthesis have made a breakthrough in the management of the bleeding disorders and has made significant changes in affected patients' life quality. On the other side, with the advent of new anticoagulants, prophylaxis, and management of thrombotic events, as a leading cause of morbidity and mortality, has both improved significantly. Direct thrombin inhibitors (DTIs) and factor Xa inhibitors (FXIs), known as direct oral anticoagulants (DOACs), have a growing role in the management of thromboembolic disorders.

Methods: Search by keywords Anticoagulation therapy, DOAC, Thrombosis management in Iran, DOAC therapy advantages,Clinical use and laboratory testing of oral anticoagulation therapy, Reversal of Anticoagulation,... in databases including PubMed, EMBASE, the World Health Organization Index Medicus for the Eastern Mediterranean Region (IMEMR WHO), Ebsco, Science Citation Index Expanded, Ovid, Google Scholar and Scopus.

Results: We reviewed related articles in these subjects which had evaluated DOAC therapy in Iran and results showed that Like most countries worldwide, in Iran, as a Middle East country, all types of anticoagulants including VKAs, heparin, and DOACs are available for management of the patients with thromboembolic disorders. Although the use of DOACs has increased in the recent years, their prescription varies between different countries. The use of DOACs, notably rivaroxaban is increasing in recent years in Iran. Apixaban has been reported as the most common DOACs in North-European and Latin American countries, but is the second most common FXa inhibitor prescribed in Iran. Routine use of DOACs, particularly rivaroxaban, can increase the prescription cost of anticoagulation therapy from 20 to 80 times in Iran. Specific antidotes of DOACs are not available in Iran, and the physicians have to use alternative choices, including PCC and FFP.

All of these issues emphasis on a more objective assessment of the current trend towards DOACs as the first-choice of anticoagulant therapy.

Conclusion: It seems that in Iran, similar to most other parts of the world, with the advent of the new anticoagulants, the overall pattern of anticoagulation therapy is shifting toward DOACs. Among, DOACs, rivaroxaban is the most commonly used anticoagulant in Iran. Dabigatran, as a direct thrombin inhibitor (DTI), is another commonly used DOAC.

Keywords: Anticoagulation therapy; thrombosis; direct oral anticoagulants

Diversity Determination of KPC- Producing Klebsiella pneumoniae Using Multilocus Variable Number Tandem Repeat Analysis (Research Paper)

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Introduction: The present study purposed at evaluating ing the genetic diversity of KPC-producing Klebsiella pneumoniae in Tehran, Iran investigated by multilocus variable-number tandem repeat analysis (MLVA).

Methods: A total of 181 isolates of K. pneumoniae were collected from different clinical samples. The antibiotic susceptibility and Modified Hodge Test (MHT) were determined according to CLSI (the clinical and laboratory standards institute) guidelines. The polymerase chain reaction (PCR) method was conducted to detect blaKPC and blaGES. K. pneumoniae isolates were typed via the MLVA method by using PCR for 8 Variable Number Tandem Repeats (VNTRs).

Results: Imipenem, with 36.5% susceptibility, was the most effective antibiotic against K. pneumoniae. 100 (55.24%) isolates had KPC positive results and 36(36 %) of them were positive for blaKPC and blaGES genes. Thirty-three MLVA genotypes were discriminated, investigation of diversity indexes (DIs) for eight loci showed that seven different alleles were the most polymorphic and the most DI was 0.349.

Conclusion: The results of the present study indicated heterogeneity among KPC-producing K. pneumoniae strains. The presence of blaKPC and blaGES in different MLVA types showed that a specific clone is not responsible for spreading the isolates and horizontal transfer occurred among these isolates.

Keywords: Klebsiella pneumoniae, Bacterial typing, Carbapenemase, MLVA, VNTR

Does platelet help cancer metastasis? (Review)

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Introduction: Cancer is including a large group of diseases that is characteristic of the cell hyperproliferation, resistance to the apoptosis; induce angiogenesis, acquisition of immortal capable and metastasis. Metastasis is a multistep process that detachment from the primary tumour, entering blood or lymph circulation, survival in circulation, colonization and metastasis formation in distance organs. Metastasis is the main leading of death from cancer and also an enormous challenge in cancer patients' treatment.

Methods: Published articles were reviewed if published in the scientific literature between 2000 and 2020. Searches were conducted using Pub Med, Scopus and Google Scholar databases. Search terms included Mesh term,"platelet cancer", and "platelet metastasis" metastasis cancer metastasis".

Results: Platelets play a major role in the hemostasis and coagulation process. Platelets enfold malignant cells and prevent their cytolysis by NK cells. Release platelet's α-granule contents (TGF-β), resulted in a transition epithelial to a mesenchymal cell that helps to promote extravasation. Interaction platelet-cancer cells lead to platelet spreading, release their granules and microparticle. Microparticles are extracellular vesicles that contain growth factor, cytokine, mRNA and miRNA. They can induce or repression of different RNA in tumours cells. However, many anti-cancer drugs development but due to high metastasis capable some cancer once remain poor prognosis.

Conclusion: Hence, more knowledge about metastasis mechanism and platelets role in this subject can help to discover ways for a halt it. This review will discuss the platelet role in cancer spreading.

Keywords: Platelet, cancer, metastasis

Does smoking affect salivary FRAP in patients with periodontitis? (Research Paper)

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Introduction: Periodontal diseases in smokers are 2.6 to 6 times higher than non-smokers and their response to treatment is much lower. Reducing levels of antioxidants and consequently increasing oxidative damage in the pathogenesis of periodontitis is effective. Regarding the importance of free radicals in the pathogenesis of periodontal diseases, the aim of this study was to investigate the effect of cigarette on the oxidative and antioxidant status of saliva in chronic periodontitis patients and compare it with healthy controls.

Methods: In this case-control study, 20 patients with chronic cigarette smoking periodontitis, 20 patients with non-smoking chronic periodontitis and 20 healthy individuals who had no history of periodontitis and smoking, were among those referring to dental clinics and clinics of Karaj were chosen. Uninstivated saliva was collected and salivary total antioxidant capacity was measured using a kit in saliva. Statistical analysis was performed using ANOVA.

Results: Total antioxidant capacity of saliva in smoker periodontitis and non-smoker periodontitis was significantly ($P < 0.05$) less than normal Persons.

Conclusion: Based on the results of this study, chronic periodontitis reduces the total antioxidant capacity of saliva, on the one hand, due to the increased production of oxidants in inflammatory responses to this disease, and, on the other hand, the presence of compounds such as nicotine cigarette that disturbs the chain Respiratory mitochondria and increased oxidants.

Keywords: Periodontitis, Cigarette, Total Antioxidant Capacity, FRAP, saliva

Does the HPV vaccine have side effects or other cons? A systematic overview (Review)

Somayeh Nikkhah,[1,*]

1.

Introduction: The human papillomavirus (HPV) affects nearly 80 millionTrusted Source people in the United States. Some of its types can cause medical concerns, from genital warts to cervical cancer.The HPV vaccine is a safe and effective vaccine that can protect children and adults from HPV-related diseases. In this study, we investigated the possible side effects of the HPV vaccine.

Methods: In this systematic review was performed using the key words HPV vaccine AND side effects in Scopus, PubMed, ScienceDirect, Google Scholar, Iranmedex databases, Until March 2020, and finally 18 articles were examined in this regard.

Results: The HPV vaccine protects against some types of HPV-related cancers and and genital warts. HPV vaccination demonstrated that the vaccine is as safe as any other vaccination. Most people receive the HPV vaccine without having any serious side effects. Mild to moderate side effects occur more often but are still uncommon. Mild to moderate side effects can include: pain or swelling at the injection site, slight fever, headache, fatigue, muscle pain, joint pain, fainting, nausea vomiting, pain in the abdomen, diarrhea. The vaccines don't prevent all HPV related cancers, only some. Therefore, it's vital that women still get a routine Pap test to check for any signs of cervical cancer. The vaccines don't protect against other sexually transmitted infections (STIs) or treat existing HPV-related illnesses or infections. It is necessary need to use condoms or other barrier methods during sex to help prevent contracting or transmitting STIs. The HPV vaccine does not affect fertility and may improve fertility in some women who've been exposed to STIs.

Conclusion: The studies support that people who receive this vaccine are not at a higher risk of any negative events.

Keywords: HPV Vaccine- Side Effects – Protection

Down-regulation of LncRNA Growth Arrest-Specific transcript 5 (GAS5) in Iranian breast cancer patients (Research Paper)

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Introduction: Breast cancer (BC) is the most common malignancy and cause of cancer-related mortality among women, in Iran. Studies have suggested that the dysfunction of long non-coding RNAs (LncRNAs) is correlated with breast cancer. In this study, we aimed to investigate the role of LncRNA Growth Arrest-Specific transcript 5 (GAS5) in breast cancer.

Methods: Human samples Breast Cancer blood specimens were collected from 30 patient women and 30 normal women. At first total RNA were extracted and after that they were removed to cDNA. At last the expression level GAS5 (Growth Arrest-Specific transcript 5) was quantified by Real Time PCR.

Results: In blood patient samples of breast cancer, GAS5 LncRNA quantified and compared with normal samples. It was shown that the level of GAS5 LncRNA expression was significantly down-regulated.

Conclusion: dysregulation of LncRNA expression level is a major component in carcinogenesis. Down-regulation of GAS5 LncRNA has previously been reported in several types of cancers. In our study, GAS5 LncRNA was down-regulated in Iranian breast cancer patients compared to normal controls. In conclusion, GAS5 LncRNA could consider as a prognostic biomarker for breast cancer.

Keywords: LncRNA, GAS5, Real Time PCR, Breast Cancer

Drugs and atural compounds against human coronavirus (Review)

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Introduction: According to recent findings that the coronavirus uses angiotensin-converting enzyme 2 as its receptor, Converting enzyme 2 (ACE2) and angiotensin-renin system inhibitors may be involved in the treatment of severe respiratory disease. A number of herbal medicines and natural compounds have human antiviral effects (HCoVs) and provide a rich source for the development of new antiviral drugs.

Methods: Ren-San-Du-Bai-Shen (Gensing to eliminate toxins) may curb the formation of cytokine storms. And by regulating chemokine, increasing blood oxygen saturation, signal transducer, and activator Transcript and ... be effective in the treatment of COVID-19. The s protein at the surface of the cov particle membrane is responsible for binding to the host cell and fusion of the virus membrane during infection. Extracts of the red blood cells Eucalyptus globulus and Flos Japonica conicera, as well as Rb1-ginsenoside, have been reported to have antiviral activity against COV-SARS due to their ability to interfere with glycoprotein envelope processing. In particular, saikosaponin B2 has strong anti-cov activity by influencing the process of viral penetration, binding, and penetration By disrupting viral glycoproteins. Emo Clin A flavonoid isolated from Rhizoma et Radix Rhei is able to block CoV-SARS through the involvement of protein S and ACE2, It is also anti-inflammatory, anti-proliferative, and anti-cancer. Depending on the dose of Emodin, asthma can be improved by inhibiting the polarization of active macrophages and STAT6 phosphorylation of airway inflammation. Scutellarein is another plant-derived flavonoid that has an anti-inflammatory effect by suppressing the expression of cyclooxygenase 2 and nitric acid Synthases induced by inhibition of the _NF_KB pathway. desaminotyrosine (DAT) The microbial metabolite was able to protect the host against influenza by suppressing interferon-1 signaling and enhancing lung immunopathology. DAT is produced by human intestinal bacteria from flavonoids and amino acid metabolism. Flavonoids have a good anti-inflammatory effect. Excessive inflammation and cytokine-related lung damage may rapidly increase pneumonia in patients with severe influenza, so the protective effect of DAT against influenza may be related to the anti-inflammatory effect of flavonoids. TCM can regulate immune cells and cytokine production in relation to immune responses. Proper immune regulation helps maintain the homeostasis of the immune system, protecting the body against infection or other harmful substances. Because it has the properties of multiple components and multiple targets and pathways for the treatment of diseases, it has great potential for the treatment of COVID-19. Dihydrotanshinone is a natural compound isolated from Salviae Miltiorrhizae Radix and Rhizoma commonly used in TCM. Dihydrotanshinone has an inhibitory effect on the entry of the MERS-CoV virus with an IC50 value of 1 μg/mL. Boenninghausenia sessilicarpa (Rutaceae) It is a plant rich in coumarin, which is traditionally used to treat fever, pus, and tonsillitis. Leptodactylone, extracted from B. sessilicarpa has a strong protective effect against virus-infected cells and anti-SARS-CoV activity with an inhibition rate of

60% per 100mg/ml. Bis-benzylisoquinoline alkaloids-tetrandrine from Stephania Tetrandrae Radix dramatically suppresses HCoV-OC43 proliferation by targeting S protein. Lian-Hua-Qing-Wen LHQWC is a common drug that improves clinical symptoms such as fever, cough, fatigue, and shortness of breath in patients with COVID-19. VAL has antiviral effects on different cell types at non-toxic doses And reduces the titers, viruses, and cell genome of the virus. VAL may reduce the toxin toxicity of the drug while having antiviral activity in vivo and showed an inhibitory effect on the proliferation stage of the poliovirus life cycle. And also has other mechanisms against the replication of the envelope virus. And inhibited the activity of LCMV and VRNP LASV, which are responsible for directing RNA genome replication and gene transcription. Valinomycin is a potential antiviral agent against coronaviruses. Flavonoids, Lonicerae, and resveratrol also have anti-inflammatory effects.

Results: Western medicines are used to treat COVID-19 patients, These drugs usually contain a wide range of antibiotics, antivirals, corticosteroids, or a combination of these and can also quickly control the main symptoms of the disease but may cause severe side effects, while TCM treatment is less toxic.

Conclusion: Ideally, an effective CoV vaccine is essential for inducing strong moral immunity with an immune cell. New technology pathways include RNA vaccine, subunit vaccine, viral vector vaccine, and DNA vaccine. CoVs are prone to mutations and recombination during replication, and this propensity has contributed to the diversity of the coronavirus.

Keywords: Coronavirus, COVID-19, Natural compounds, Drug

Effect of amoxicillin nanoformulation on its antibacterial activity against common bacterial strains involved in nosocomial infections (Research Paper)

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Introduction: Nanotechnology offers a great chance to treat drug-resistant microbial infections. The purpose of this study was to synthesize ampicillin-encapsulated polymeric nanoparticles and compare the antibacterial activity of this nanoformulation with pure ampicillin.

Methods: Ampicillin-encapsulated polymeric nanoparticles were prepared using chitosan as a polymer and alginate as cross linking agent. The obtained nanoparticles were characterized by Fourier transform infrared, dynamic light scattering and scanning electron microscopy. The antibacterial effects of the nanoparticles were evaluated using broth microdilution and well diffusion methods against some common bacterial strains involved in hospital-acquired infections.

Results: The drug-encapsulated nanoparticles were found to be spherical in shape with average size of 81 nm. These nanoparticles had a significant antibacterial effect on all tested bacteria, except for S.aureus. They also displayed stronger antibacterial activity than the nanocarrier alone or free antibiotic. The highest mean zones of growth inhibition (24.5 mm) for methicillin-sensitive Staphylococcus aureus and the smallest zone (13.6 mm) for the resistant species of this bacterium were determined. MIC of the nanoformulation against these two strains was respectively determined at 1.5 asnd 48 µg/ml and for E.coli and S.aureus at 6.6 and 256 µg/ml

Conclusion: The results suggest that ampicillin encapsulation in polymer nanoparticles has the potential to increase its antibacterial activity against bacteria causing nosocomial infections.

Keywords: Ampicillin, Antibacterial activity, Hospital infections, Nanoformulation.

Effect of CAR T-cell Therapy in Acute Lymphoblastic Leukemia (Review)

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Introduction: Acute lymphoblastic leukemia (ALL) is one of the most common leukemias in children and the elderly. Chimeric antigen receptors (CAR) have great potential in the treatment of acute diseases. Recent advances in the immune system have led to the development of new therapies, such as the use of car Tcell, and the treatment of patients with refractory or recurrent acute lymphoblastic leukemia. In this type of treatment, immune T cells are collected from patients and designed to make car T cells and re-injected into the same patient. This type of treatment is an innovative form of treatment that puts cluster of differentiation 19 (CD19) at its most advanced. In this article we investigate the effect of therapeutic CAR T cells in the treatment of acute lymphoblastic leukemia.

Methods: We searched Pubmed,Google Scholar,SID,Cochrane databases for articles from last 5 years with treatment Car T Cells and Acute Lymphoblastic Leukemia keywords.By searching these databases 97 articles in Pubmed,234 articles in Google Scholar,10 articles were found in Chocrane. Out of a total of 341 articles, 301 were exclude after reading the headlines. Also with reading abstracts we exclude 21 articles. Finally we include 19 articles into the our study.

Results: 12 articles showed that the use of CD 19 CAR T cells therapy has been effective in the treatment of ALL disease. In 3 articles, according to clinical studies, there is a possibility of recurrence of the disease after recovery with this treatment. And in other articles no effectiveness was observed. Studies show that patients who did not respond to a CAR T cell had an abnormal composition in their CD 19 exon. An article stated that one of the concerns in CAR T cell therapy is tumor resistance. This means that exposure to therapeutic antibodies may result in a recurrence of the effect. In another article, it was stated that many efforts have been made to build suitable car T cells for the treatment of patients who may not be suitable for other treatments due to lymphobenia. Reports also indicate that CAR T cell show exceptional activity against bcell malignancies, which can indicate ALL in the early stages.

Conclusion: The results show that the use of CAR T Cells is one of the most effective and durable types of treatment for acute lymphoblastic leukemia, but due to lack of experience in this method and for more accurate and complete recovery, more studies are needed. This method requires further study. This method also increases the patient's survival time.In treatment with car t cells, environmental factors affecting the immune system's response to this treatment should be investigated. Other related treatments may also interfere with the healing process.

Keywords: Treatment, Car Tcells, Acute lymphoblastic leukemia

Effect of granulosa secreted factors on oocyte development and blastocyst quality in goat (Research Paper)

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Introduction: Natriuretic peptide type C (NPPC) is synthetized by granulosa cells and binds to natriuretic peptide receptor 2 (NPR2) that mostly present in cumulus cells. NPR2 activation induces the synthesis of cyclic guanosine monophosphate (cGMP), which is transferred via gap junctions from cumulus cells to the oocyte. cyclic guanosine monophosphate has inhibitory action over phosphodiesterase 3A (PDE3A), maintaining high concentrations of cAMP in the oocyte and sustaining meiotic arrest. In the other hand, prostaglandin E2 (PGE2) belongs to a group of signaling molecules that mediate many important reproductive processes, including ovulation, implantation, maintenance of luteal function, and establishment of pregnancy. Prostaglandin E2 is also involved in ovulation cascade events, including the expansion of cumulus cells and the expression of proteases associated with follicle rupture. In these processes, PGE2 indirectly mediates LH action or directly acts on the expression of ovulatory genes, including Amphiregulin (AREG), act on EGF receptor (EGFR) and activate the extracellular signal-regulated protein kinases 1 and 2 (ERK1/2), protein kinase C (PKC) pathways and other signaling pathways in granulosa and cumulus cells (CCs), which make the COCs competent to respond to Luteinizing hormone (LH) surge. The aim of this study is whether critical deficiencies of in vitro maturation related to a lack of granulosa cell-COC communication in human and other species like goat.

Methods: In this study we evaluated the effect of NPPC, AREG and PGE2 on goat oocyte to in vitro development and embryo quality. At first, goat COCs were aspirated from slaughterhouse ovary, washed and exposed for 8 hours to NP (1000 nM), after that exposed to different concentration of PGE2 (0.1nM, 1nM and 10nM) + AREG (300 nM). TCM and conventional medium were considered as control

groups. We assessed in vitro development of these goat oocyte by in vitro fertilization and blastocyst quality with differential staining.

Results: In this study, the proportion of oocytes reaching the blastocyst stage on Day 7 in NP◊PGE2 (1nM) + AREG showed no difference with control and other groups. In contrast, we indicated that blastocyst rate in the 0.1 nM and 10 nM PGE2 and TCM dramatically decreased compared with conventional group. The analysis of the cell number of blastocyst showed that there were not significantly differences in the treated groups NP (1000 nM) ◊ PGE2 (0.1, 1 and 10 nM) + AREG (300nM) compared to the control groups.

Conclusion: According to our previous study PGE2 solely might not control the processes which occurs during oocyte maturation in the goat. This study indicated that selection of the best concentration of NP, PGE2 and AREG could be positive effect on maturation, development rate and blastocyst quality compare with TCM and/or conventional group.

Keywords: Goat, Oocyte, Natriuretic peptide, Prostaglandin E2, Amphiregulin.

Effect of Herbal Medicines on Treatment of Lung Cancer (SCLC and NSCLC) (Review)

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Introduction: Lung cancer is the most commonly diagnosed cancer. An estimated 1.8 million novel lung cancer patients happened in 2012, accounting for approximately 13% of total cancer diagnoses. Lung cancer is classified into two groups of small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). There are various treatment methods for lung cancer treatment based on its type. Among such methods are chemotherapy, radiotherapy, surgery, gene treatment, palliative cares. Each of these methods can be used either individually or in combination with other methods for lung cancer treatment. However, sometimes this common therapy methods are not enough and appropriate to treatment of lung cancer. Therefore, it is necessary to use an effective treatment method as an alternative or complementary treatment method. Herbal medicines have been utilized in Oriental countries for centuries as tonics. Several beneficial effects of herbal medicines on cancer have been reported. Herbal medicines can be used along with radiotherapy, chemotherapy and surgery in treatment of NSCLC and SCLC. This treatment method lead to increase efficiency and decrease side effects of common treatment method including chemotherapy. In this review we focused on properties of the herbs, which are useful in therapy of NSCLC and SCLC.

Methods: In this review we used online database such as NCBI (PubMed), and Google scholar. This Research is the result of a survey of more than 82 articles of which 44 articles are directly used in this study.

Results: Medicinal herbs can considerably decrease tumor size without side effects and also they can reduce lung cancer related pains. In addition, this treatment method as single therapy method and also adjunctive therapy can be used in the treatment of NSCLC and SCLC. For example, Plumbagin, shogaol-6, Radix Sophorae flavescentis, ai-kang, Glycorrhiza glabra (GLYC) and Olenandria diffusa (OLEN) are group of medicinal plants which are useful in treatment of SCLC. Moreover, Cassiae Ramulus Cinnamomi, Paeoniae Rubrae, raw Radix Glycyrrhizae Uralensis, Officinalis Recens Zingiberis rhizome, Radix Scutellariae Baicalensis, Fructus Zizyphi Jujubae are containing cantharidin and plumbagin which led to inhibit of cell division of NSCLC.

Conclusion: Herbals have potential therapeutic value for patients with advanced NSCLC and SCLC. Additionally, herbals medicine has been reported to have different advantageous effects to improve survival rate, and quality of life of patients with lung cancer. As a result, using this treatment can be useful in treatment of NSCLC and SCLC.

Keywords: lung cancer, NSCLC, SCLC, chemotherapy, medicinal herbs

Effect of Hypothyroidism in Cardiovascular System (Review)

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Introduction: Hypothyroidism is defined as an elevated serum level of thyroid stimulating hormone (TSH), with free thyroxine (FT4) or triiodothyronine (FT3) levels within or below the reference range common in the general population. Increasing number of studies have indicated that thyroid hormones may play an important role in the maintenance of cardiovascular homeostasis under physiologic and pathologic conditions. It is also involved in modulating cardiac contractility, heart rate, diastolic function, and systemic vascular resistance, thereby affecting cardiac function. Thyroid dysfunction is a risk factor of cardiovascular disease.

Methods: In the current study, key words including hypothyroidism, thyroid-stimulating hormone, thyroxine and cardiovascular disease were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar over the past two decades and the desired data was organized.

Results: Thyroid hormones have a variety of effects on the cardiovascular system that can greatly impact cardiac function. Hypothyroidism is associated with decreased cardiac output due to the impaired relaxation of vascular smooth muscle and decreased availability of endothelial nitric oxide. This produces a cascade effect of increased arterial stiffness that leads to increased systemic vascular resistance. On a molecular level, these alterations result from the reduced expression of sarcoplasmic reticulum Ca2+-ATPase and increased expression of phospholamban, which inhibits ATPase. Thyroid hormones also impact the renin-angiotensin-aldosterone system. Hypothyroidism decreases cardiac output, increases systemic vascular resistance, decreases arterial compliance, narrows pulse pressure, increases diastolic pressure, atherosclerosis, increases risk of coronary artery disease, decreases nitric oxide production, decreases vascular smooth muscle relaxation, decreases cardiac contractility and decreases vascular smooth muscle relaxation.

Conclusion: It is clear that thyroid hormones play a significant role in regulating cardiac, vascular, and metabolic physiology. Physiologic alterations from both overt and subclinical hypothyroidism have varied cardiovascular effects and treatment may reverse some, if not all, of the effects. There is evidence to suggest that treatment of mild dysfunction can improve cardiovascular outcomes.

Keywords: Hypothyroidism, cardiovascular disease, thyroxine, thyroid-stimulating hormone

Effect of in ovo application of tetracalcium phosphate-containing polymeric scaffold on chicken embryo development (Research Paper)

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Introduction: Chick embryo chorioallantoic membrane (CAM) is well known as a powerful experimental tool for the study of normal and pathologic angiogenesis and chicken embryo development, due to its high vascular network. Additionally, CAM is an embryonic tissue lacking an immune system and having mesenchymal cells with stem-like potential able to differentiate depending on a specific microenvironment (Cirligeriu et al. 2018). Calcium (Ca) is an essential mineral which its vital roles (e.g. blood coagulation, bone formation, and nervous system) in the body are clear (Tuan et al. 1986). However, the injection of hydroxyapatite nanoparticles was not reflected in embryo growth and even slowed down bone development (Matuszewski et al. 2020). Biochemical approach is one of the Current techniques for enhancing the formation of vascular networks. This technique involves the incorporation of the small bioactive molecules or growth factors within scaffolds for promoting formation of the blood vessels which can prepare ideal nutrition for the embryo (Saik et al. 2011). Polymeric tissue-engineered scaffolds are the best candidate for delivery of molecules or other factors. The objective of the present study was to evaluate the effect of in ovo application of ion delivery from tetra-calcium phosphate-containing polymeric scaffold on chicken embryo development.

Methods: Fabrication of composite scaffold The preparation of TTCP is fixed to solid-state reaction of calcium carbonate and dicalcium phosphate anhydrate at high temperatures. Then 0.4-gram TTCP was incorporated in a hydroxyethyl cellulose/hyaluronic acid/gelatin scaffold which was previously fabricated by (Derakhshani et al. 2020). CAM assay Fertilized eggs were purchased from a local company and the assay was performed as (Moreno et al. 2016) protocol.

Results: On day 8th, to study the chick embryo development, the eggs were evacuated. Fig.2 showed the scaffold treated chicken embryo(STCE). As shown in Fig. 2(a) the vitelline membrane covers almost the whole yolk. Eye pigmentation is readily visible. The beak's upper and lower parts are differentiated (Fig. 2(b)), as well as the wings and legs. The neck stretches and the brain is completely settled in its cavity. Also, we can see the external auditory canal is opened. Additionally, the claws are formatted and the budding of first feather follicles are invisible (www.thepoultrysite.com). The last two phenomena belong to day 9th of the normal chick embryo development, but all of them happened on day 8th of STCE. The comparison of height (control=2.1 cm, STCE=3.3 cm) and weight (control=0.67 g,

STCE=1.7 g) of control and STCE are depicted in Fig.3 and Table 1. The results indicated the presence of scaffold and released tetra-calcium phosphate ions (especially Ca, which is effective in cell proliferation) had a positive effect on chicken embryo development.

Conclusion: In this study, we prepared a polymeric scaffold that released inorganic ions such as calcium. The CAM assay indicated that the released ions positively affect chicken embryonic development and this approach is more effective than direct injection of a calcium phosphate member.

Keywords: tissue engineering, CAM assay, ion delivery, scaffold

Effect of Lactobacillus bacteria on Serum Level of Vitamin D in an Animal Model of Experimental Encephalopathy (Research Paper)

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Introduction: Recently, the use of probiotics has attracted the attention of any researchers as a way to prevent and treat immune system diseases through increased uptake of protective factors. The aim of this study was to evaluate the potential of Lactobacillus bacteria (LB) isolated from dairy products to treat an animal model of experimental encephalopathy and their effect on vitamin D serum level.

Methods: A total of 90 pasteurized and traditional dairy product samples were collected from different regions of Fars province. The samples were cultivated in MRS agar medium and different biochemical tests were used to Lactobacillus isolates. Molecular detection was performed using the 16S rRNA gene by FLB 190 and RLb 190 specific primers. Forty-eight male Wistar rats were divided into 6 groups (n = 8 per group). Cuprizone (CPZ) was used to induce demyelination in the treatment groups. Afterward, Lactobacillus isolates were administered (1 × 10 9 cfu/g) by gavage to the treatment groups for 30 days. Finally, different groups underwent motor tests (beam walking test, grid-walking test, pendulum test) and biochemical tests (vitamin D 3 , B 12 and malondialdehyde assays). Serum levels of vitamins D 3 and B 12 were determined by ELISA test and malondialdehyde assay by Rao method.

Results: The lactobacilli isolated from dairy products included Lactobacillus acidophilus (3.22%), Lactobacillus plantarum (12.9%), Lactobacillus casei (25.8%), Lactobacillus sakei (3.22%), Lactobacillus rhamnosus (3.22%), Lactobacillus pentosus (3.22%), Lactobacillus curvatus (3.22%), and Lactobacillus buchneri (6.45%). In this study Lactobacillus acidophilus, actobacillus plantarum and Lactobacillus casei were used for the treatment of experimental ncephalopathy. There was significant difference in serum level of vitamin D 3 in the experimental and revention groups compared to the sham group after one month of treatment. Moreover, the prevention roup showed a significant increase in vitamin B 12 compared to the experimental group I.

Conclusion: Lactobacilli can reduce the MS symptoms by increasing the serum levels of vitamin D 3 and B 12 . The bacteria also have antioxidant properties that reduce the level of free radicals and thereby prevent the deleterious effect of CPZ on the corpus callosum region of the brain. Based on histopathologic findings, myelin healing increased during the treatment period and tissue density was evident in the treatment group. Malondialdehyde was also reduced as a substance that is involved in the antioxidant process. Therefore, the studied lactobacilli are useful in the treatment of MS.

Keywords: Lactobacillus, Multiple Sclerosis, Cuprizone, Behavioral Test, Vitamin D 3 and B 12 , MDA.

Effect of lubricant gel on the length of the first stage of labor and perineal trauma in primiparous women (Research Paper)

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Introduction: Perineal injuries are caused following natural vaginal delivery. These injuries have short and long term complications. Episiotomy in the short term causes the complications .Researchers are looking for strategies to reduce the use of episiotomy. According to new investigations, the usefulness of episiotomy has been obscured.

Methods: This study is a randomized controlled trial that includes all primiparous women who referred to Iranshahr Iran hospital for normal delivery from March 2016 to February 2017. A total of 110 primiparous women were randomly assigned to the two groups of using lubricant gel and control. In the intervention group, during cervical dilatation of 4 cm until complete cervical dilatation, 5 ml of water-soluble lubricant gel was used at each vaginal examination. In the control group, routine care was performed.

Results: The mean length of the first and second stage of labor were significantly different between intervention and control groups. In the intervention group, the frequency of healthy perineum was 61.8%(n=34) episiotomy and perineal trauma was 38.2%(n=21) and in the control group, these values were 14.5%(n=8) and 85.5%(n=47) , respectively. Two patients in the intervention group and 3in the control group had grade II perineal tears. In the control group, only 5 cases of grade III perineal tears were reported, but no cases of grade 4 perineal tear were reported in two groups.

Conclusion: It seems that using lubricant gel during the first phase of the active phase of labor is a suitable strategy to reduce the length of the first stage of labor, the number of episiotomy and perineal trauma.

Keywords: Lubricant gel, Delivery length, Perineal trauma,Primiparous

Effect of Nigella Sativa on Cadmium-Induced Toxicity in Colorectal Cancer (Review)

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Introduction: Toxic heavy metals such as cadmium (Cd) may change the gut microbiome composition and increase the risk of colorectal cancer (CRC). Cd inhibits the growth of certain intestinal flora and re-shaped the community of gut microbiota both at the phylum and genus levels, increases pathogenic bacteria and decreases protective commensal bacteria (such as Lactobacillus); disrupts tight junctions, increases gut permeability, and bacterial translocation. This condition may develop resistance to antibiotic drugs. However, some agents with anti-bacterial properties can be used for targeting pathogenic flora in CRC. Nigella sativa (N.S) as a medicinal plant, traditionally used for reducing the risk of chronic diseases such as cancer due to its antibacterial and antioxidant properties. This review discusses how N.S may effect on Cd toxicity and pathogenic antibiotic resistant bacteria in CRC.

Methods: Relevant studies in electronic databases were selected by searching MEDLINE Library. Only relevant English published articles were included.

Results: Available evidence suggested that N.S exerts a protective effect against Cd toxicity and dysbiosis in CRC through the following mechanisms. Phenolic components of N.S have antibacterial properties against gram-positive and gram-negative bacteria. This medicinal plant scavenges free radicals, prevents cell damage from oxidative substances, improves the activity of anti-oxidative enzymes, chelates Cd, reduces and inhibits cadmium accumulation and alters the levels of beneficial metal ions in the body. On the other hand, N.S disrupts cell membrane of pathogenic bacteria and makes it more permeable, resulting in reducing pathogenic bacteria. N.S prevents intestinal epithelial barrier disruption and bacteria translocation, and increases probiotics bacteria, which can absorb, sequestrate and remove Cd and protect intestinal against bio accessibility of Cd.

Conclusion: N.S may attenuate toxicity of Cd in CRC through cadmium detoxification and beneficially reshape gut microbiota profiles, from dysbiosis to eubiosis.

Keywords: Nigella Sativa, Cadmium, Colorectal Cancer

Effect of Physical Activity on gene expression in cancer (Review)

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Introduction: There are significant epidemiological evidences that regular physical activity or exercise reduce the risk of developing diseases such as cardiovascular disease , diabetes and some types of cancers. Exercise also affects the function of our genes such as increases of methylation. Gene expression studies may be a sensitive tool to characterize the early effects of exercise on immune regulation.

Methods: To review the effect of Physical Activity on gene expression in cancer we conducted a bibliography research using sources from PubMed, and websites of institutions like Cancer Research the WHO.

Results: Moderate exercise can exert a number of effects on the body such as improving insulin sensitivity in addition to lowering blood pressure. Vigorous exercise causes damage to the muscle resulting in disarrangement in fiber structures, loss of fiber integrity, and secretion of muscle protein. There are several hypothesized biological mechanisms involved in the association between physical activity and cancer risk, including an effect on adiposity, endogenous sex and metabolic hormones, chronic inflammation, oxidative stress, and genomic instability . Then it is increase or decrease the risk of cancer.

Conclusion: Therefor changes in Physical Activity have a high impact on reducing the signaling pathways thus ,it is reducing the risk of cancer.

Keywords: Physical activity . Moderate exercise . Vigorous exercise. Gene expression . Inflammation .cancer.

Effect of Pore Structure and Morphology of Titanium Foams on Their Biological Behavior in Hard tissue replacements (Research Paper)

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Introduction: Porous titanium has appropriate mechanical and biological properties and may be a promising choice for hard tissue replacements. In this literature, the effect of the pore structure of titanium foams was studied.

Methods: for this purpose, someones were fabricated by powder metallurgy of titanium hydride and by using the space holder method. Three types of space holders were used: sodium chloride with cubic morphology, urea with needle shape, and sphere morphology.

Results: The space holders played a key role in the pore structure as confirmed by microstructural observations. Also, the influence of various pore morphologies on the human primary osteogenic sarcoma cell line (MG63) was evaluated in vitro.

Conclusion: The results show that the proliferation abilities of MG63 were related to different pore morphologies of such porous scaffolds. These results may guide the design for porous titanium in bone defect restoration.

Keywords: titanium foam, pore morphology, biological behavior

Effects of Adrenocorticotropic hormone therapy as a treatment in patients with multiple sclerosis: A Systematic Review (Review)

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Introduction: Background and Objective: The use of Adrenocorticotropic hormone (ACTH) in chronic diseases such as multiple sclerosis is a new treatment that has become widely used today. In most studies, this method has been associated with increasing the quality of life of patients. However, the use of this method is less common among physicians and few MS health practitioners are trained in ACTH. The objective of this systematic review was to evaluate the effects of This treatment method (using ACTH) in the recovery of patients with this problem.

Methods: Methods: Data sources: we used Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library) PubMed/MEDLINE, EMBASE, CINAHL, Google Scholar, Scopus, Web of science and ISI. All studies with Inclusion criteria and keywords ACTH; adrenocorticotropic hormone; multiple sclerosis; treatment were collected from these sources. Review methods: All identified articles from different sources were transferred to a database using resource management software to remove duplicates. Two reviewers independently examined the titles and abstracts of the articles using the inclusion criteria checklist (Human Studies, All randomized controlled trials (RCTs), quasi-experimental randomized controlled trials (quasi-RCTs), cluster randomized trials, case-control and before and after studies containing drug interventions). In case of disagreement between the two, the judgment regarding the inclusion of the article in the study was applied with the opinion of a third reviewer. The PRISMA (Preferred reporting items for systematic review and metanalyses) flowchart is used to present the selection process, which shows how studies enter and exit the systematic review. Articles were reviewed for quality with the help of CASP (Critical Appraisal Skills Programs) tool. The emphasis will be on the methodology of the articles and the biases (selection, performance, identification, attrition, reports) were evaluated.

Results: Results: The number of studies collected according to the inclusion criteria was 259, which after removing duplicates the number of remaining records after eliminating duplicate studies was 131. Finally sixteen studies assessed for eligibility as the main articles. Number of patients involved in our main studies was 541. Reducing the rate of T-lymphocyte in the peripheral blood and serum IgG in cerebrospinal fluid (CSF) and in the blood (significant decrease) was the result of

the immune system suppression by ACTH. ACTH injection significantly reduced peripheral blood CD4 + T cell ratio at 2, 6 and 12 months after treatment but no change was observed in CD3 + T cells. Three weeks of ACTH treatment improved patients' visual function, recorded by flash VEPs. Alopecia, nausea and vomiting, and minor infections were the most common complications. The use of this method can positively affect the course of chronic progressive MS in most patients, but a treatment method does not cause permanent improvement and some kind of maintenance therapy or re-treatment is needed.

Conclusion: Conclusion: As a result, medication regimen with this hormone can be effective in improving patients' performance, slowing the progression of the disease and creating an outpatient period to maintain recovery. However, more empirical studies (larger intervention population) are needed to accurately express the effectiveness of this method.

Keywords: Keywords: ACTH; adrenocorticotropic hormone; multiple sclerosis; treatment

Effects of breastfeeding and formula feeding on the expression level of FTO, CPT1A and PPAR-α genes in healthy infants (Research Paper)

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Introduction: The prevalence of obesity and subsequent chronic diseases is increasing worldwide. Breastfeeding in comparison with formula-feeding has desirable effects on the prevention of obesity, chronic and infectious diseases. The aim of this study was to investigate the expression level of fat mass and obesity-associated (FTO), carnitine palmitoyltransferase IA (CPT1A) and, peroxisome proliferator-activated receptor-α (PPAR-α) genes in peripheral blood mononuclear cells (PBMC) of breastfed, formula-fed and mix-fed (breastfed plus formula-fed) infants.

Methods: A total of 150 infants participated in this case-control study. All subjects were healthy infants aged 5 to 6 months that divided into 3 groups; breastfed, formula-fed and mix-fed. The expression level of FTO, CPT1A and, PPAR-α genes in PBMC were evaluated in each group using reverse transcription-polymerase chain reaction (RT-PCR) method.

Results: Our findings showed that the current weight, height and, head circumference of infants in the formula feeding and mix feeding groups were significantly higher than the exclusive breastfeeding group. The expression level of FTO and CPT1A genes in formula-fed and mix-fed infants were significantly up-regulated ($p<0.001$) than breastfed infants, while the expression level of PPAR-α gene was significantly down-regulated ($p<0.05$).

Conclusion: Breastfeeding showed modulatory effects on the expression level of obesity- predisposing genes and protects against obesity and subsequent non-communicable diseases. However, more investigations are required to explain the epigenetic effects of breast milk.

Keywords: : breastfeeding, formula feeding, FTO, CPT1A, PPAR-α

Effects of common herbal extracts on chemotherapy-induced nausea and vomiting: A systematic review (Review)

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Introduction: Introduction: Cancer is one of the major problems of the health system, as it is the third leading cause of death in Iran after cardiovascular disease and accident. One of the side effects of chemotherapy is nausea and vomiting, which in acute conditions can have a major impact on quality of life, nutritional status, length of hospital stay, interruption of treatment, and severe infections. Unfortunately, there is still definitive treatment to relieve and eliminate It does not exist. Due to the side effects of chemical drugs and the resistance of some cancer patients to these drugs, one of the important approaches in the treatment and prevention of vomiting is the use of plant extracts. The aim of this systematic review was to investigate the effects of common herbal extracts on nausea-vomiting due to chemotherapy.

Methods: Methods: The present systematic review was a review and used as a library study method and search for content from electronic and indexed sources including Iran medex, Google Scholar, Pubmed, SID with the keywords Cancer, Chemo therapy, Nausia, Vomiting, vegetal extract and 120 articles. Was obtained. Among these articles, the full text of the articles, which were available and published in the last five years, were further reviewed.

Results: Results: Studies have shown that many of these plant extracts inhibit vomiting nausea in patients undergoing chemotherapy by acting on the neurotransmitters serotonin, dopamine, histamine and muscarinic acid and also by acting on the brain stem.

Conclusion: Conclusion: Considering the economic problem and the side effects of chemical drugs, the use of plant extracts with less side effects can be a suitable alternative for the treatment and prevention of vomiting nausea in cancer patients undergoing chemotherapy.

Keywords: Keywords: Cancer, Chemotherapy, Nausea, Vomiting, Plant Extract

Effects of coronavirus on the human body (Review)

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Introduction: Coronavirus belongs to the subfamily corinavirinae in the family Coronaviridae of the order Nidovirales and this subfamily consists of 4 genera: gammacoronavirus, alphacoronavirus, deltacoronavirus, betacoronavirus

Methods: Sore throat, runny nose, in less common cases sputum, headache, myalgia or fatigue, chest pain, diarrhea leading to dehydration with devastating effects. Anorexia is the most common gastrointestinal symptom. Nausea and vomiting and diarrhea are less common, Common symptoms include fever, cough, and respiratory symptoms. The virus is transmitted through aerosols, contact with infected people and surfaces , and the virus is found in the urine and feces of infected people has been. A significant decrease in the total number of lymphocytes indicates that the coronavirus consumes many immune cells and inhibits the function of the body's cellular immune system. Damage to T lymphocytes is an important factor in exacerbating the disease. Receptor binding expressed by host cells is the first stage of viral infection, followed by fusion with the cell membrane. It is argued that lung epithelial cells are the main target of the virus. Human-to-human transmission of COV-SARS has been reported to occur by binding between the receptor-binding domain of the Virus spike and the cell receptor, which occurs as the angiotensin 2 (ACE2) receptor conversion enzyme. Most importantly, the receptor-binding domain sequence of 19-COVID spikes is similar to COV-SARS. These data suggest that entry into host cells is most likely via the ACE2 receptor. The mortality rate is directly related to diabetes, obesity, smoking, old age, chronic heart disease, kidney transplantation, kidney failure, liver cirrhosis and chronic lung disease, hypertension, and hyperlipidemia. These people are more susceptible to the coronavirus due to a weakened immune system. People with diabetes are at risk for infections, especially the flu and With good glycemic control, this risk, although not completely eliminated, is reduced. Obstructive sleep apnea occurs in 40% of obese people, which is associated with systemic hypertension, pulmonary hypertension, and heart disease caused by the lungs. Patients with renal insufficiency due to excessive ururia, neutrophil dysfunction, malnutrition, trace elements deficiency, overdose Iron deficiency, impaired glucose metabolism, hyperparathyroidism, and the use of immunosuppressive drugs to treat and control major diseases lead to increased mortality from infections. Some patients with COVID-19 develop severe pneumonia, pneumonia, ARDS, or multiple organ failure. Lymphocyte counts decreased in most patients in COVID-19, indicating that the disease mainly affects lymphocytes, especially T lymphocytes such as SARS. The virus particles, which spread through the respiratory mucosa and infect other cells, induce cytokinin storms in the body, trigger a series of immune responses, and They cause changes in peripheral white blood cells and immune cells such as lymphocytes. Some patients progress rapidly to ARDS and septic shock, which is eventually associated with multiple organ failure. When the virus multiplies in lung tissue, it causes alveolar proliferation and interstitial inflammatory exudation, edema, and the formation of clear membranes. As a result, differences in alveolar

gas exchange cause hypoxia in the CNC, increasing anaerobic metabolism in the mitochondria of brain cells. Acid accumulation can cause dilation of cerebral arteries, swelling of brain cells, interstitial inflammation, obstruction of cerebral blood flow, and Even headache caused by ischemia and cramps, If hypoxia goes unnoticed, cerebral edema and circulatory disorders may worsen dramatically. With intracerebral hypertension, the brain gradually deteriorates, and drowsiness, onion conjunctivitis, and even coma are observed. In addition, in patients at particular risk for brain disease, hypoxia may lead to acute brain disease such as acute ischemic stroke. Patients with 19-COVID often suffer from severe hypoxia.

Results: Hypoxemia damage may cause further damage to the nervous system. Nervous system damage from a viral infection may be mediated by the body's nervous system. The pathology of severe viral infections is closely related to the development of systemic inflammatory response syndrome (SIRS). SIRS can start abnormally in pneumonia due to coronavirus infection, while early anti-inflammatory intervention effectively prevents immune system damage and reduces the risk of damage to the nervous system.

Conclusion: In some patients, sputum fills the lungs in the form of a jelly-like substance, which makes it difficult for the patient to breathe due to the accumulation of these substances in the lungs, and they need artificial respiration. Therefore, early detection and hydration are of particular importance.

Keywords: coronavirus, COVID-19, SIRS, hypoxia, nervous system, apnea ,diabetes,

Effects of Immediate and Delayed Exercise on balance activities in the Experimental Traumatic Brain Injury in male rats. (Research Paper)

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Introduction: Following our previous studies on effects of exercise on brain edema and motor behavior following traumatic brain injury(TBI) , This study was designed to examine changes in effects of immediate and delayed exercise on balance activities in a rat model of in TBI

Methods: which male rats were divided into 5 groups:1) Non-exercise group: (NE): Rats that did not enter the exercise, 2) Sports Group: (24A): the exercise initiated 24 hours after TBI, and continued for 4 weeks , 3) Exercise group: (1WA): the exercise initiated 1 week after TBI, and continued for 4 weeks, 4) Exercise group: (1MB): the exercise initiated 1 month before TBI, and continued for 4 weeks ,5) Exercise group: (1MBA): the exercise initiated 1 month before TBI, and continued for 1 month (4 weeks) after it . TBI was induced by the Marmarou method and evaluate the balance activities by Rotarod test.

Results: The recovery was indicated significantly affected by the exercise in TBI groups. Post hoc analysis demonstrated the improving in balance performance in animals that returned to exercise immediately (24A), and exercise 1MBA were higher (117.71+1.19) ($P < 0.05$), than those that experienced 1 week delays(1wA) (90.01+1.44) in their return to running, or previous exercise(1MB)(56.25+0.99) ($P < 0.05$), but not for animals in the No-exercise group ($P < 0.001$).

Conclusion: The present results indicated that exercise may cause an improvement of balance activities after TBI.

Keywords: TBI, exercise, balance activities, Rotarod test.

Effects of in-vitro copper nanoparticles on common bacterial strains involved in nosocomial infections (Research Paper)

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Introduction: In recent years, bacterial resistance to antibiotics has increased at an alarming rate. On the other hand, the rate of discovery of new antibiotics has not been able to keep pace with the emergence of resistance. Therefore, there is a need for new approaches to combat bacterial infections. We investigated the antibacterial properties of copper nanoparticles (Nps of copper) in most bacterial strains responsible for nosocomial infections.

Methods: The effect of copper nanoparticles on in vitro growth of standard and clinical strains of Escherichia coli, methicillin-resistant Staphylococcus aureus (MRSA), Enterococcus faecalis, Klebsiella and Pseudomonas aeruginosa was investigated. Copper nanoparticles with an average diameter of 20 nm were produced using the arc evaporation method. The minimum inhibitory concentration (MIC) and the minimum antibacterial concentration (MBC) were determined and the antibacterial effects were compared with the common antibiotics used to treat these strains, ie the disk diffusion method.

Results: Arc-fabricated copper nanoparticles were successfully synthesized. At 50 A, transmission electron microscopy (TEM), X-ray diffraction (XRD), and scanning electron microscopy (SEM) showed analysis of the fabrication of relatively pure, scattered, brown Nps with an average size of 23 nm. Escherichia coli and MRSA showed acceptable levels of sensitivity to copper Nps. The effects of copper nanoparticles were more effective than cephalexin in suppressing Escherichia coli colony formation, while Cu Nps was more effective in suppressing MRSA growth than vancomycin. Other strains showed resistance to copper Nps.

Conclusion: The use of copper nanoparticles may be a good way to treat or prevent infections caused by Escherichia coli or MRSA.

Keywords: Copper nanoparticles, Antibacterial, Bacterial resistance

Effects of Myrtle methanolic extract on protoscoleces during hydatid cyst surgery (Research Paper)

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Introduction: Hydatid disease [cystic echinococcosis, CE] is a parasitic infestation by a tapeworm of the genus Echinococcus [6]. Surgery is considered the first choice of treatment for CE [7]. The use of effective scolicidal agents during CE surgery is necessary to reduce the risk of intraoperative spillage of the cyst contents [protoscoleces] and subsequently recurrence of CE and secondary infection [8, 9]. The present scolicidal agents have indicated various side effects such as liver necrosis and sclerosane colangitis [10]. This investigation aims to evaluate the protoscolicidal effects of Myrtle (Myrtus communis L.) extract against protoscoleces of hydatid cysts on in vitro model.

Methods: Protoscoleces were aseptically aspirated from the livers of naturally infected sheep. Various concentrations of myrtle extract (62.5, 125, 250, and 500 mg/mL) were used for 10-60 minutes. Eosin exclusion test was used to determine the viability of protoscoleces.

Results: The results revealed that extract at the concentrations of 500 and 250 mg/mL killed 100% protoscoleces after 10, 20 minutes of exposure. Moreover, all of the protoscoleces were killed after 30 and 60 minutes of exposure to 125 and 62.5 mg/mL concentration of extract, respectively. The mortality rate of protoscoleces in the negative and positive controls was 9.1% after 60 min and 100% after 10 min of exposure, respectively. The obtained results demonstrated all the concentrations of extract had significant ($p<0.05$) protoscolicidal effects compared with the control group.

Conclusion: The obtained results demonstrated all the concentrations of extract had significant ($p<0.05$) protoscolicidal effects compared with the control group.

Keywords: Cystic echinococcosis; Prtotoscoleces; Extract; natural product

Effects of natural compounds incorporated into electrospun nanofiber mats in wound healing (Review)

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Introduction: The crucial role of skin as a shield membrane against any external factor which can cause infection is undeniable. Wounds caused due to various incidents can be acute or chronic based on their intensity. The area surrounding the acute wound is responsible for repairing the sore caused via the release of two kinds of signaling molecules - cytokines and growth factors. Inasmuch as chronic wounds can be deeper, they have a longer and more complicated healing process. Generally, wound healing is a dynamic process involving harmonious biochemical and physiological stages, that occurs over the sequential yet overlapping phases of inflammation, proliferation, and remodeling. It synthesis new tissue for regenerate or repair of skin. The number of cells involved in wound healing that can be mentioned are: platelets, inflammatory cells, fibroblasts, endothelial cells, epidermal cells and keratinocytes. In order to minimize side effects as well as speeding up of wound recovery, choosing the best wound restoration strategy is a principle. Some methods have used to wound healing are moist dressing treatment method, vacuum therapy, laser therapy, electrotherapy, platelet-rich plasma (PRP) therapy, ozone therapy, cell therapy, gene therapy and nanotechnology. In this review, the effects of natural products combined with polymeric nanofiber scaffolds in wound healing were studied.

Methods: Since that nanofibers display an extremely high surface to volume ratio, nanoscale structure and high porosity, also are suitable and biodegradable for drug delivery and targeting, they can be utilized to deliver drugs to attain either localized therapy or controlled release of the drugs at the target. Drugs can be combined with polymeric nanofiber scaffold implants to prevent infection at that specific site as the tissue regeneration occurs. It is proved that, Propolis has antiseptic, anti-inflammatory, anti-microbial, anti-tumor, anti-ulcer, anti-fungal, regenerative, antioxidant and etc. properties and is organic antibiotic. In addition, this herbal medication stimulates cell proliferation, collagen formation and tissue repair, and it treats faster injured tissue; It doesn't cause toxicity and allergies in the body and is safe. Furthermore, Aloe vera and Calendula officinalis with antimicrobial and anti-inflammatory properties as well as ability to collagen synthesis and angiogenesis are used to repair damaged tissue objectives.

Results: According to the results of various researches that have been conducted in these fields, the viability of investigated fibroblast cells was increased with increasing these natural compounds concentration and incubation time, that indicate regeneration properties of mentioned compounds and their role as a fibroblast growth stimulator.

Conclusion: However, more extensive in vivo research is needed to perform in this field as long as it can be tested on humans directly.

Keywords: Wound healing; Nanofiber; Natural compound; Fibroblast

Efficacy of Using probiotic lactobacilli with Antagonistic Activity against Pathogens of Wound Infections (Research Paper)

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Introduction: Burns are the most common type of trauma with a high mortality rate worldwide. Using modern and natural medicines, especially probiotic products have recently been regarded for cutaneous wounds healing. The present study was designed to investigate the effects of Lactobacillus plantarum and Lactobacillus casei on wound healing and antimicrobial activity of two probiotic lactobacilli against P. aeruginosa.

Methods: In this study, Anti-adhesion activity considered by the glass slide method and the Anti-adhesion substances in cell-free supernatant (CFS) were quantified by the HPLC method.. After induction of the second-degree wounds, MDR P. aeruginosa injected subcutaneously directly on the burn. The animals were divided into 5 groups. The supernatants were sprayed for treatment every day and the evaluation of wound healing was conducted

Results: Based on our findings, lactobacilli bacteria exerted good anti-adhesion effects on P. aeruginosa which HPLC analysis indicated that their inhibitory effect can be due to their main organic acids. The effect of treatments on fibroblastic cells showed that the treated group by supernatants of L. plantarum and Lactobacillus casei had the most number of fibroblastic cells compared with the non-treated group. Moreover, the bacteria increased the rate of fibroblastic cells, re-epithelialization in the wound area and the largest thickness of the epidermis and dermis layers. Antimicrobial activity of lactobacilli bacteria against MDR P. aeruginosa was determined by prevents infection.

Conclusion: These findings showed that probiotic bacteria specially significantly reduced inflammation and they can treat a P. aeruginosa infection in a second-degree burn.

Keywords: Wound healing, Cutaneous wound, Probiotics, Burns, P. aeruginosa

Electrospun bioactive polycaprolactone/Brushite biocomposite for bone tissue engineering applications (Research Paper)

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Introduction: Tissue engineering has developed several methods for repairing and replacing damaged tissue using biological factors, cells, and biological scaffolds.

Methods: In this study was used dicalcium phosphate dehydrate (brushite) as Bone phase mineral precursor in different amount of weight percentage (0%, 1%, 3%, 5%, 10%) in combination with biocompatible polymer, poly caprolactone (PCL), In order to reinforce the physical, biochemical, biological and mechanical properties by electrospinning. The adhesion, viability, proliferation, and differentiation of mesenchymal stem cells derived from the human bone marrow (hMSC) on scaffolds were investigated using electron microscopy (SEM), MTT assay, live-dead assay, alizarin red staining, alkaline phosphatase activity assay, osteocalcin (OCN) gene expression analysis by Real-time PCR. The morphology and mechanical properties of scaffolds were characterized, using SEM and tensile strength test and the bioactivity of the scaffold in stimulated body fluid (SBF) was assessed.

Results: The results showed that PCL-DCPD 3 wt% had the highest tensile strength (15.35 MPa) and indicated a significant increase in compared with pure PCL. Furthermore, hMSC seeded on scaffolds after 1, 3, 7 days showed over 80% viability. Alkaline phosphatase enzyme activity of cells on PCL-DCPD 3 wt% in compared with pure PCL was increased. In addition, the osteocalcin (OCN) gene in the 3% DCPD scaffold showed a 6.1- fold increase in expression compared to pure PCL.

Conclusion: It is concluded That electrospund PCL- DCPD scaffolds with optimum concentration can be proper candidate for bone tissue engineering application.

Keywords: scaffold, electrospinning, tissue engineering, polycaprolactone, dicalcium phosphate dehydrate

Electrospun Poly (ε-caprolactone)/Tio2 nanocomposite scaffolds for bone tissue engineering application; In-vitro study (Research Paper)

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Introduction: Electrospinning is a widespread technique used in the tissue engineering field, due to the fabrication of nanoscale/microscale fibrous structures similar to the native extracellular matrix morphology. Polycaprolactone (PCL) is biocompatible aliphatic polyester with high potential usage in medical applications. On the other hand, Gelatin (GE) type A is used as an additive in order to increased nanofibers degradation and hydrophilicity, and also improve solution viscosity. In this study, nanofibrous scaffolds based on PCL/Ge containing TiO2 nanoparticles were fabricated by the electrospinning method. The main objective of this study is to investigate the effect of Tio2 NPs on human mesenchymal stem cell-derived bone marrow, in terms of cytotoxicity, releasing reactive oxygen specious (ROS), adhesiveness, and survival. the advantageous properties of Tio2 NPs such as light weight, bioactivity, biocompatible, antibacterial, corrosion protecting have made it an interesting material to be considering in compositing with polymers. The results demonstrated that the addition of TiO2 NPs improved the mechanical strength, hydrophilicity, and cellular attachments of scaffolds.

Methods: In this study, we blended nanofibrous scaffolds based on PCL/Ge (75/25 proportion) into 9:1 acetic acid/ formic acid solvent, that dissolve about 24 h before electrospinning. These parameters and electrospinning conditions are identical. Titanium dioxide nanoparticles (Tio2 NPs) presenting percentages through the solution is the only applied scaffolds electrospun discrepancy. The main object is the investigation effect of Tio2 NPs on scaffold properties and behavior of human mesenchymal stem cells-derived bone marrow, especially in terms of cytotoxicity, reactive oxygen specious (ROS) generation, adhesiveness, survival.

Results: The results demonstrated that the addition of TiO2 NPs improved the mechanical strength, hydrophilicity, and cellular attachments of scaffolds. And because of the advantageous properties of Tio2 NPs, it potentially could be used in future regenerative applications.

Conclusion: The results of anisotropic(randomly) structurally form of PCL/GE/Tio2 NPs fibers that are similar to the basal structure of bone tissue, hence electrospun fibrous scaffolds would be opened the possibility of using in future experiments about bone tissue engineering and regenerative medicine.

Keywords: tissue engineering; Electrospinning; Tio2 nanoparticles, nanomaterial

Emerging Function and Clinical Significance of hsa_circ_0065173 in peripheral blood of breast cancer patients pre and post chemotherapy in order to find potential biomarker related to response to treatment (Research Paper)

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Introduction: Breast cancer remains one of the most frequently diagnosed gynecological malignancies, currently accounting for 29% of all new cancer cases, and is the second leading cause of cancer-associated mortality in females all over the world. Early diagnosis, radical surgery and adjuvant therapy have improved the survival rates and prognosis of breast cancer patients, however mortality rates remain high. In order to maximize the effectiveness of therapy, it is important to understand the molecular pathways involved in the pathogenesis of breast cancer that cause metastasis and chemotherapy resistance. Recently, high-throughput transcriptome analysis shows that protein-coding genes make up only about 2% of the human genome, while the vast majority of the human genome encodes large amounts of noncoding RNAs (ncRNAs) that includes: long non-coding RNA (lncRNA) , micro RNA (miRNA), and circular RNA (circRNA), which are characterized by covalent closed loops. CircRNA are formed by back-splicing without 3'-end and 5'-end, unlike lncRNA. Circular RNA (circRNA) is a key regulator in the development and progression of human cancers, however its role in breast cancer tumorigenesis is not well understood. The present study aims to investigate the expression profiles and potential modulation of hsa_circ_0065173 in peripheral blood of breast cancer patients pre and post-chemotherapy in order to find the potential biomarkers related to treatment response.

Methods: Total RNA was isolated from the peripheral blood samples before and after chemotherapy using TRIzol reagent following the manufacturer's protocol. RNA was reverse transcribed into cDNA using M-MLV Reverse Transcriptase. SYBR Green Real-time RT PCR using special primers for circ-RNA hsa_circ_0065173 and beta-actin as an internal control was performed. All the values were standardized with 2-ΔΔCt method and statically analyzed using Graph Pad Prism 8.2 software.

Results: hsa_circ_0065173 was upregulated in peripheral blood samples of breast cancer patients compared with normal control. In addition, hsa_circ_0065173 upregulation was associated with lymph node involvement. After receiving the first dose of chemotherapy, the expression level of hsa_circ_0065173 decreased significantly.

Conclusion: In conclusion, hsa_circ_0065173 has an oncogenic function and correlates with advanced clinicopathological features and unfavorable survival. hsa_circ_0065173 might function as a prognostic biomarker for breast cancer patients pre and post-chemotherapy and might be a therapeutic target for the treatment of breast cancer in the future. Advanced related researches will be promising in cancer management.

Keywords: Breast cancer, hsa_circ_0065173 , chemotherapy, prognostic biomarker

Endometrial expression of αvβ3 Integrins could be affected by Chlorpyrifos (Research Paper)

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Introduction: Integrins are the key molecules that induce proper bonding between the fetus and the uterus in the window of the implantation process. The goal of this analysis was to determine whether Chlorpyrifos (CPF), as a global pesticide, can have an impact on integrin alpha v and beta 3 in this process.

Methods: Thirty female NMRI mice were randomly picked and split into three CPF, sham, and control groups. Following 6 weeks of CPF injections in the experimental group and DMSO as diluted CPF in the Sham group, all groups were mated. All the mice euthanized on the 5th day of gestation. Genes and proteins of endometrial integrins (αv and β3) studied using real-time polymerase chain reaction (RT-PCR) and immunohistochemistry methods. Besides, the mouse liver was fixed in 10% formalin for Masson's trichrome staining.

Results: Based on the findings, fibrosis of the liver increased in the CPF group compared with the others. The proportion of genes' expressions of integrin subunits declined by the effect of CPF, while there was not any notable consequence on mice in the sham group. Alpha v and beta 3 integrin proteins expressed in all groups, but the concentration of these proteins in the CPF group was lower than in other groups.

Conclusion: This study found that the (3mg/kg) of CPF causes fibrosis in the liver and downregulate of αv and β3 integrins expression. Changing these patterns of proteins could have numerous influences on unsuccessful implantation. Therefore, this longitudinal research suggests that a detailed analysis of the impact of insecticides can be key to the unrecognized cause of infertility in women.

Keywords: CPF, endometrium, integrins αvβ3

Epidemiological study of SARS, MERS, COVID-19 coronavirus families in global pandemics (Review)

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Introduction: Coronavirus disease 2019(COVID-19) is a rapidly spreading epidemic that, like the outbreak caused by two other pathogenic respiratory coronaviruses (sars –cov and mers-cov), often causes severe infection, mainly through respiratory droplets. It is reported that it was first discovered in Wuhan, China, in people who were exposed to seafood, with a mortality rate of 2.27%. According to the World Health Organization and epidemiological studies, more than thirteen million people worldwide have been infected and more than one million have died so far (Sars, Mers, Covid-19) in global pandemics.

Methods: This study was conducted in 2020 by searching for keywords such as corona virus family and global pandemics in reputable databases such as: pub med and google scholar. Finally, 15 articles were found, of which 10 articles were used

Results: Based on studies from articles, the results show that this disease was first discovered in Wuhan, China in people who were exposed to seafood. Symptoms of this disease include fever, dry cough and fatigue, and so far more than thirteen million. People in the world are infected with this disease and more than one million people die and in terms of genome sequence from 75 to 80% is the same as SARS-CoV. Its treatment agents include plasma therapy, which is the best way to improve the recovery rate of patients. To control the prevalence of COVID-19 early detection and reduced close contact is the best way to prevent the disease. Reducing Secondary Infections Among Medical Staff Knowing the genome sequence facilitates rapid detection of the virus Rapid response The Chinese Clinical and Scientific Public Health Associations facilitate the recognition of clinical diseases and a basic understanding of the epidemiology of infection.

Conclusion: According to the findings, it is better to set up a risk reduction program that is not a risk factor for us and it is recommended that we continue to do the treatment process and proper protection to do a good job of testing COVID-19.

Keywords: corona virus family and global pandemics

Epidermal growth factor and three-dimensional scaffolds provide conducive environment for differentiation of mouse embryonic stem cells into oocyte-like cells (Research Paper)

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Introduction: Three-dimensional (3D) culture provides a biomimicry of the naive microenvironment that can support cell proliferation, differentiation and regeneration. Moreover, due to the importance of biomaterials in tissue engineering, successful emulation of tissues depends on the introduction of essential biomolecules, such as growth factors to develop tissue-like constructs. Some growth factors, such as epidermal growth factor (EGF), facilitate normal meiosis during oocyte maturation in vivo. In this study, a scaffold-based 3D co-culture system, using purified alginate was applied to induce oocyte differentiation from mouse embryonic stem cells (mESCs).

Methods: Mouse embryonic stem cells were induced to differentiate into oocyte-like cells using embryoid body (EB) protocol in the two-dimensional (2D) or 3D microenvironment in-vitro. To increase the efficiency of the oocyte-like cells differentiation from mESCs, we employed a co-culture system using ovarian granulosa cells in the presence or absence of epidermal growth factor (+EGF or –EGF) for 14 days and then the cells were assessed for germ cell differentiation, meiotic progression and oocyte maturation markers

Results: The cultures exposed to EGF in the alginate-based 3D microenvironment, showed the highest level of premeiotic (Oct4, Mvh), meiotic (Scp1, Scp3, Stra8, Rec8) and oocyte maturation (Gdf9, Cx37, Zp2) marker genes ($P<0.05$) in comparison to other groups.

Conclusion: Our data highlight the importance of tissue engineering approach in differentiation of ESCs to oocyte-like cells, and supplementation of EGF is effective in improving the differentiation process. The expression of specific genes related to premeiotic, meiotic and oocyte maturation, accompanying Oct-4, Stra8 and Mvh protein expression confirms the synergistic effect of EGF and alginate-based 3D culture condition in oocyte differentiation.

Keywords: Growth Factor, Alginate, Scaffold, Embryonic Stem Cells, Cell differentiation

Essential oil from Dracocephalum kotschyi Boiss, antibacterial and antioxidant activities and natural preservative effect in shelf life extension of shrimp storage (Research Paper)

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Introduction: The safety and shelf-life of food are some of the most challenging factors which food industries are currently confronted with. Several food preservation systems such as freezing, salting, and heating as well as more complicated methods like chemical and synthetic preservation and modified atmosphere packaging can be used to reduce the risk of outbreaks of food poisoning and improve the shelf-life extension of food. In recent years, the use of natural preservation methods is a field of growing interest. Essential oils (EOs) have achieved attention due to their food preservation effects, particularly for the antimicrobial and antioxidant effects. Plant essential oils contain large amounts of bioactive compounds. The antimicrobial properties of EOs are attributed to actions including their ability to disrupt cell wall and cytoplasmic membrane. The antioxidant activity of EOs is due to their potential ability to cease or suspend the oxidation reaction of organic materials in the presence of oxygen which is a result of some special components including phenols. This study was designed to evaluate the antioxidant and antibacterial, and effects of Dracocephalum kotschyi essential oil (EODK) in raw shrimp over a 7 day storage period at 4 °C.

Methods: : The hydrodistillation process was used for essential oil extraction. The yield of the oil was 0.1% and the oil was yellow. Shrimp meat was treated into different concentrations of EODK and the properties were compared to shrimp meat without any additive. Also, the chemical composition of the oil was analyzed using Gas chromatography, and the antioxidant and antimicrobial activities of EDOK were investigated.

Results: Several compounds have been identified in the essential oil. The major components found in the EODK were Limonene, α-terpineol, Caryophyllene, and perillyl alcohol. The essential oil's IC50 value of 32.35 µg/ml in the DPPH assay, could be regarded as its strong antioxidant potential. Antibacterial activities of EODK were screening against five strains, Staphylococcus aureus, Escherichia coli, Shewanella putrifaciens, pseudomonas fluorescens, and Yersinia enterocolitica by minimum inhibitory and bactericidal concentration (MIC and MBC) and disc diffusion methods. The results indicated that EODK has the highest activity against Staphylococcus aureus and Escherichia coli at the concentration of 500 mg/ml. Finally, the EODK applications as food preservatives were studied. Indeed, the effect of different percentages (0.5, 1%) of EODK for microbiological (total viable count), physicochemical parameters (pH and moisture), and sensory

testing (color, appearance, taste) of meat stored during refrigerated storage for 7 days were evaluated. The results showed that the control sample (without any EO) had the highest pH and moisture content and the difference was significant with the treatments. Treatments containing 1% had the lowest pH and humidity. The bacterial counts of samples were lower than control samples during storage ($P<0.05$) and the concentrations of 1% EO had the best inhibition of bacterial growth in shrimp meat.

Conclusion: Plants essential oils can be applied by combining with other natural preservatives for enhancing shelf-life extension of food as well as the manufacture of health-oriented products because of The antimicrobial and antioxidant effects.

Keywords: Antibacterial, Antioxidant, Essential oil, Dracocephalum kotschyi, Shelf-life extension

Ethics of belief and medical education (Research Paper)

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Introduction: The necessity to pay attention to the ethics of belief was first raised by William Kingdon Clifford, the 19th-century philosopher and mathematician. In his famous article in 1877, he indicated that a scholar is morally responsible for the beliefs he/she adopts and should accept them only if there is compelling evidence. The scholar should know that if the acceptance is not backed by persuasive evidence, it is immoral, particularly if the beliefs entail practical consequences and the consequences can cause problems and pains for others.

Methods: This is not a classic experimental study and its method is based on didactive reasoning and logical methods.

Results: In order to be able to provide their services in promoting the individual and collective public health, particularly those physicians who have direct contact with patients, physicians and other public healthcare-related staff must have sufficient knowledge (both quantitatively and qualitatively). Knowledge and episteme are the scholar's (whether physician or non-physician) very justified true beliefs. At the same time, such beliefs are directly related to people's health and illness, that is individuals' pains and suffering نتایج:In order to be able to provide their services in promoting the individual and collective public health, particularly those physicians who have direct contact with patients, physicians and other public healthcare-related staff must have sufficient knowledge (both quantitatively and qualitatively). Knowledge and episteme are the scholar's (whether physician or non-physician) very justified true beliefs. At the same time, such beliefs are directly related to people's health and illness, that is individuals' pains and suffering As a result, according to Clifford, not only the students and physicians must embrace some beliefs that are backed scientifically but since they are ethically and accountably responsible for the individuals, they must pay precise attention to accepting scientific subjects to have sufficient support.

Conclusion: In order to be able to better distinguish true scientific propositions from false and invalid ones, the physicians and students must have knowledge of critical thinking. Thus, it is their moral duty to get a grasp on critical thinking and critical thinking can improve their teaching and learning processes. In other words, the commitment to the ethics of belief both improves students' moral performance and their educational performance. ethics of belief,medical education,critical thinking

Keywords: ethics of belief,medical education,critical thinking

Evaluating expression of long non-coding RNAs SNHG7 and CRNDE-h in exosomes derived from serum and tissue samples of colorectal carcinoma (Research Paper)

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Introduction: Colorectal cancer is the third most common cancer and the second leading cause of cancer death in the world. This cancer is prevalent in men more than women and unfortunately its age has fallen. Metastasis is one of the important reasons why people with colorectal cancer do not live. Extensive studies have been conducted on non-coding RNAs in different cancers. The RNAs that are transcript are not translated.

Methods: also examined two long non-coding RNAS called SNHG7 and CRNDE-h in this cancer. The expression of these two in tumoral and normal colon and rectal tissues in patients with colorectal cancer. Also, this comparison was carried out on serum levels of patients with colorectal cancer and normal individuals.

Results: Exosomes are vesicles that are secreted from different cells into the target cell and create a positive or negative change in that cell. These vesicles have proteins and types of RNA, which can sometimes be a good biomarker for cancer detection.The results showed that the expression of SNHG7 and CRNDE-H increased in colorectal cancer, which suggests that they are oncogene.

Conclusion: According to the data we can introduce these two long-term RNA non-coding code as a suitable biomarker for colorectal cancer.

Keywords: colorectal cancer, long noncoding RNA, exosome , biomarker

Evaluating the anti-inflammatory effect of conditioned medium derived endometrial stem cells in endometriosis women (Research Paper)

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Introduction: Introduction. Although, the endometriosis is a benign inflammatory disorder, it mainly causes complications. Thus, trials for better diagnosis and treatment seems necessary. It is supposed that mesenchymal stem cells derived from menstrual blood (MenSCs) in endometriosis patients are different from that of healthy women and so, they are responsible for the creation of the disease. According to the high expression of inflammatory factors in MenSCs of endometriosis patients, it was supposed that the conditioned medium of these cells from healthy women can affect the expression of inflammatory genes. The aim of this study was evaluating the expression of inflammatory genes in endometriosis patients under treatment of conditioned endometrial from MenSCs of healthy women.

Methods: Methods. Menstrual blood samples (1-2 ml) were collected from endometriosis women and healthy women as control group, in the age range of 22-35 years. Isolation of MenSCs from two groups was performed by the Ficoll-Paque density-gradient method and then endometriosis-derived MenSCs were treated with conditioned medium from control group in passage three. The expression of inflammatory genes including IL-1α, COX-2, TNF-α, NF-kB and HIF-1α were assessed using real time RT-PCR.

Results: Results. Endometriosis-derived MenSCs were morphologically different from healthy MenSCs and also showed higher expression of CD10 marker, which experienced significant decrease in CD10 marker after 4 days' treatment with conditioned medium of healthy MenSCs. Also, after treatment, Endometriosis-derived MenSCs showed significant decrease in TNF-α and NF-kB expression but no significant decrease in HIF-1α.

Conclusion: Conclusion. Down-regulation of inflammatory genes in endometriosis-derived MenSCs under treatment of conditioned medium derived from healthy MenSCs can be considered as an effective approach for the treatment of endometriosis which needs more investigations.

Keywords: Condition medium, Menstrual blood-derived stem cells, Endometriosis, Inflammatory genes

Evaluation of resistance to methicillin and the presence of mecA and pvl genes in the Staphylococcus aureus has been isolated from Valiasr Hospital in Tabriz (Research Paper)

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Introduction: Methicillin-resistant Staphylococcus aureus (MRSA) is a cause of staph infection that is difficult to treat because of resistance to some antibiotics. Pantone valentine leucocidin PVL is one of the important toxins of this bacterium that causes the walls of host white leucocytes lysis and cause necrosis in the tissues.Various studies have suggested that strongly connection between PVL with MRSA. The aim of this study was to determine the frequency of methicillin resistance and to search for mecA and pvl genes in Staphylococcus aureus isolates isolated from Valiasr hospital in Tabriz.

Methods: In this descriptive cross-sectional study, 142 specimens were collected from the patients with initial diagnosis of Staphylococcus aureus and were identified using standard laboratory tests. Isolate resistance to common antibiotics was measured by disk diffusion method and resistance to methicillin was measured by cefoxitin disk method. The presence of mecA and pvl genes in the isolates was evaluated using specific primers and PCR.

Results: From all samples, 98 isolates were identified as Staphylococcus aureus. The highest antibiotic resistance was observed against penicillin with 96.2% and the lowest resistance to cotrimaxazole with 16% Multiple antibiotic resistance of MDR was present in 62% of isolates. 26 isolates were identified as methicillin resistance by phenotypic method. The MECA gene was identified in 13 isolates, which were identified by phenotypic method 11 as MRSA isolates and 2 as methicillin-sensitive isolates. No pvl gene was found in any of the isolates.

Conclusion: The results of this study showed high and multiple resistance of Staphylococcus aureus to the antibiotics studied. 26% of the isolates were MRSAs, which should be considered a serious issue in different parts of the hospital.

Keywords: Staphylococcus aaureus, Methicillin Resistance, mecA, pvl

Evaluation of antibiotic resistance in Enterococcal strains isolated from gram-positive clinical specimens (Research Paper)

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Introduction: Enterococci are gram-positive microorganisms that are one of the most important causes of mortality in hospitalized patients and more than common causes of UTI. Enterococcus can persist or widespread in the hospital environment and to obtain antibiotic resistance indices. The importance of these bacteria has increased the ability to transmit resistance genes to other microorganisms and their role as a resistance scattering reservoir.

Methods: This study aimed to rate the prevalence and frequency of Enterococci strains among Gram-positive strains isolated from patients hospitalized in Shohada and Motahari hospitals in Gonbad.

Results: The results have shown that out of 120 samples Gram-positive strains collected from hospitals, 10 isolates are Enterococci. As well as, antibiogram test results by the disk diffusion method shown high resistance of much isolate to current antibiotics(Penicillin, Norfloxacin, Tetracycline, Cefoxitin, Nitrofurantoin, Trimethoprim, Rifampin, and Gentamicin).

Conclusion: the importance of Enterococci is their intrinsic resistance and the ability to quickly get resistance mechanisms to antibiotics against almost all available antibiotics. Today the resistance and their ability of these bacteria to be transmitted to other Genus have become a matter of concern.

Keywords: Isolation, Enterococcus, clinical infection, Antibiogram

Evaluation of antibody titer from the chimeric protein of lethal factor and protective antigen of Bacillus anthracis encapsulated in PEG-PLA diblock copolymer nanospheres (Research Paper)

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Introduction: Anthrax is a particularly dangerous infectious disease that affects humans and livestock. It is characterized by intoxication, serosanguinous skin lesions, development of lymph nodes and internal organs, and may manifest itself in either a cutaneous or septic form. The pathogenic agent is Bacillus anthracis, a gram-positive, endospore-forming, rod-shaped aerobic bacterium (Schmidt et al., 2011; Ahmadi et al., 2015). Due to the production of heat resistant spores, very high mortality, easy production and distribution and also creating respiratory, gastrointestinal, cutaneous diseases and its potential use in biological warfare, B. anthracis is one of the most important fatal biologic agents (Knight, 2001; Ahmadi et al., 2015). The principal virulence factors of B. anthracis consist of an anti-phagocytic capsule composed of poly-Dglutamic acid (PGA) and a secreted bacterial toxin. The anthrax toxin, which is predominantly responsible for the etiology of anthrax, belongs to the family of bacterial binary ABtype toxins, which consist of a receptor-binding B subunit known as the protective antigen (PA) and two catalytic A subunits, i.e., the lethal factor (LF) and edema factor (EF). Protective antigen is combined with either LF or EF to form the lethal toxin (LeTx) and edema toxin (EdTx), respectively (Okinaka et al., 1999; Koehler, 2009; Schmidt et al., 2011; Honari et al., 2014). Currently, the standard approach for anthrax therapy is to kill the germinating bacilli by administering aggressive antibiotics. However, antibiotic therapy is ineffective once systematic anthrax symptoms appear because by that time, fatal concentrations of the anthrax toxin have accumulated in the patient's body (Schneemann and Manchester, 2009) and the emergence of antibiotic-resistant strains as a result of natural evolution or intentional modification by genetic engineering also poses a new challenge to traditional antibiotic treatment (Gilligan, 2002; Gilligan, 2004). Therefore, the development of an antitoxin for combined use with antibiotic therapy is a top priority. Current vaccines for human administration are prepared in England and the United States based on cell extract deposition (Pannifer et al., 2001). The production of the new generation of anthrax vaccines has focused on various recombinant expression systems (Gorse et al., 2006; Campbell et al., 2007; Brown et al., 2010; Bellanti et al., 2012; Reed et al., 2015). Studies have shown that antibodies generated against four regions of PA (PAD4) are capable of neutralizing anthrax toxin (McComb and Martchenko, 2016). On the other hand, PA mixed with LF has been shown to increase the specific antibody response to PA (Pezard et al., 1995; Price et al., 2001). Chimer proteins are a product of recombinant DNA technology and have attracted the attention of researchers due to their special applications. One of the most important applications of recombinant chimeric proteins is their use as vaccines and drugs [104-103]. Nanotechnology has evolved rapidly in recent years. Due to recent advances in materials science and nanoengineering, nanoparticles have received much attention for applications in

biology and medicine. In medicine, nanomaterials are used in applications such as scaffolding and tissue equipment engineering, targeted drug delivery systems, cancer treatment, and clinical diagnosis and treatment. In recent years, significant efforts have been made to use nanotechnology to deliver drugs and vaccines [113]. Polymeric nanoparticles (NPs) are solid colloidal particles with diameters of one to one thousand nanometers that are composed of large molecular weight materials and can be used in therapeutic applications, as an adjuvant in a vaccine, or as a drug carrier. One of the first reports of the use of polymer nanoparticles in the treatment of cancer dates back to 1979, when the uptake of anticancer drugs into polyalkyl cyanoacrylate nanoparticles was studied. Polymers used to form nanoparticles can be synthetic or natural. These nanocarriers have been used for various applications such as drug delivery, imaging, and apoptosis diagnosis [124]. The most important advantages of using polymer nanoparticles in conducting antigen are: Continuous release of antigen Controlled release for a specified period and ….[135]. The purpose of this study was to express the lfD1-pa4 gene of B. anthracis in Escherichia coli expression strain, purify the recombinant protein,encapsulated in PEG-PLA diblock copolymer nanospheres and produce polyclonal antibody in mice and compare the encapsulated lethal factor domain 1-protective antigen 4 (LFD1-PA4) fusion protein and nonencapsulated lethal factor domain 1-protective antigen 4 (LFD1-PA4) fusion protein.

Methods: Expression of recombinant protein The recombinant LFD1 - PA4 protein expressed and purified as described elsewhere by this laboratory [18]. Encapsulation of mixed proteins and chracterization LFD1 - PA4 proteins was encapsulated by w/o/w method (15). To investigate the size and zeta potential of the nanoparticles produced, the Malvern model DLS device made in England, belonging to Baqiyatallah University of Medical Sciences, was used. Evaluation of Antibody titration of Encapsulated and non Encapsulated LFD1 -PA4 proteins (LFD1 - PA4) NonEncapsulated LFD1 -PA4 protein were injected four times (20, 15, 10, 10µg respectively) combined with the VAX-ORIENT IPA-70 Adjuvant, Pars Company, and Encapsulated LFD1 - PA4 proteins were injected one times (first day) and two time (first and twenty-eighth day) Without Adjuvant. Finally the blood samples were taken from the mice and antibody titration evaluated by ELISA [16-18].

Results: Expression and purification of the LFD1 -PAD4 protein Selected colonies were cultured in a LB medium at 37 °C, after reaching logarithmic growth, the expression induced by 1 mM IPTG at final concentration. The expression and quality was evaluated by 12% SDS-PAGE gel .The LFD1and PAD4 protein band was indicated at 48 kDa.(Fig.1). Encapsulation of mixed proteins and chracterization The results of PEG-PLA nanoparticles loaded with chimeric protein(LFD1 - PAD4) by DLS are shown in the table1 and diagram1. Evaluation of antibody titration against recombinant protein by indirect ELISA An indirect ELISA was used to analyze the antibody titration and to characterize its ability to detect antigens in each injection phase. Blood samples were randomly taken from test and control mice, one week after the second, third, and fourth injection with LFD1-PA4 (fusion) (encapsulated and nonencapsulated proteins). After serum isolation, ELISA was performed. The antibody titration is shown in Diagrams 2. Figure 1 - Purification of proteins from Ni column: Column 1) Before Ni column, Column 2)

Sample containing proteins (Flow) collected from Ni column, Column 3) Buffer C collected, Column 4) Buffer D Group Collected, columns 5 and 7) collected buffer E, column 6) protein marker column 8) collected MES buffer Table (1) Investigation of physicochemical properties of nanoparticles using dynamic light diffraction پتانسیل زتا (میلی ولت) اندازه (نانومتر)PDI CONTROL -32.1 13.88 0.337 ENCAPSULATED -23.1 93 0.280 Diagram 1- PEG-PLA nanoparticle size distribution range containing LFD1 - PAD4 chimer protein under optimal Diagrams 2-ELISA curve of IgG antibody production after each injection of chimer protein LFD1 - PAD4 in three forms of free (A), loaded one injection (B) and loaded two injections (C)

Conclusion: The present vaccines against anthrax are based on PA such as anthrax vaccine adsorbed (AVA) in USA and anthrax vaccine precipitated (AVP) in Britain. The usage of the traditional AVA or the second-generation of recombinant protective antigen vaccine ((rPA)-based vaccine) is not ideal because multiple injections are required over a long period. Besides, neither AVA nor an rPA-based vaccine is suitable for the post-exposure vaccination in persons who have been freshly infected with B. anthracis (Aulinger et al., 2005; Bouzianas, 2010). Recent studies on anthrax showed that LF is important and necessary for development of effective vaccines (Hepburn et al., 2007). Moreover, production of antibodies (toxin neutralization antibody-TNA) that cause immunity in animals are based on CD4+ T cells plays a key role in production of neutralizing antibodies, class switching and maturity of lymphocytes. After reviewing similar studies in this case and considering that the domain of lethal factor 1 at the amino terminus of the protein and PA4 are naturally located at the carboxylic end of the protective antigen, finally the chimeric protein LFD1-PA4 was selected.[46,153,152,151].In this research lfd1-pa4 synthetic gene cassettes were expressed in E. coli-BL21 (DE3) PlysS cells and related proteins were purified by affinity chromatography. After encapsulation of chimeric protein in PEG-PLA diblock copolymer nanospheres , we evaluate the antibody titer produced by injecting chimer protein (LFD1- PAD4) in three forms: free (four injections), loaded (once injected) and loaded (twice injected) and calculate its amount in each injection showed that the highest antibody titer against nanoparticles loaded with chimer antigen.

Keywords: Anthrax, Antibody titer, , LFD1-PA4, polymeric nanoparticle,peg-pla

Evaluation of antibody titer from the combination of lethal factor and protective antigen of Bacillus anthracis encapsulated in PEG-PLA diblock copolymer nanospheres (Research Paper)

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Introduction: Anthrax is a zoonotic and severe infectious disease that caused by Bacillus anthracis [1, 2]. The pathogenicity of Bacillus anthracis is depends on two important factors in the production of toxins and the formation of capsules. Bacterial toxin is made from three protein components: Protective Antigen (PA) (83 kDa), Lethal Factor (LF) (90 kDa), and Edema Factor (EF) 89 kDa [3-5]. The PA protein consists of four regions where its carboxyl terminal region (region 4 or PAD4), with binding to host cell surface receptors, causes the introduction of LF and EF into the cell. On the other hand, the LF factor, which has four regions, binds to the PA through the amino-terminal region (region 1 or LFD1) [6]. Current vaccines for human use are prepared in England and the United States based on cell extract deposition [9].The production of the new generation of anthrax vaccines has focused on various recombinant expression systems [7-11]. Also, according to studies, the production of recombinant vaccines containing PA and lethal factor can be more effective in activating the immune system[12]. Today, attempts are being made to develop vaccines that contain one or more specific components of the organism. These vaccines are called subunit vaccines and have significant advantages over traditional vaccines; On the other hand, it has created more opportunities for engineering vaccines and determining the appropriate formulation to create an immune response [13]. Due to recent advances in materials science and nanoengineering, nanoparticles have received much attention for applications in biology and medicine. Polymeric nanoparticles (NPs) are solid colloidal particles with diameters of one to one thousand nanometers that are composed of large molecular weight materials and can be used in therapeutic applications, as an adjuvant in a vaccine, or as a drug carrier. The purpose of this study was to purify and encapsulated of mixed antigen (LFD1 + PAD4) in PEG-PLA double-block copolymer nanospheres and to evaluate the antibody titer in the laboratory animal.

Methods: Expression of recombinant proteins The pET 28a-lfD1 and pET28a-pa4 gene construct obtained from Department of Biological science in Imam Hossein University which described elsewhere .The recombinant LFD1 and PA4 proteins expressed and purified as described elsewhere by this laboratory [14]. Encapsulation of mixed proteins and chracterization An equal mixture of LFD1 and PAD4 proteins was encapsulated by w/o/w method (15). To investigate the size and zeta potential of the nanoparticles produced, the Malvern model DLS device made in England, belonging to Baqiyatallah University of Medical Sciences, was used. Evaluation of Antibody titration of Encapsulated and non Encapsulated LFD1 and PA4 proteins (LFD1 + PA4) Encapsulated and non Encapsulated LFD1 + PA4 proteins were injected four times (20, 15, 10, 10µg respectively) combined with the VAX-ORIENT IPA-70 Adjuvant, Pars Company, Encapsulated LFD1 + PA4 proteins were injected one times (first day) and two time (first and twenty-eighth day)

Without Adjuvant. Finally the blood samples were taken from the mice and antibody titration evaluated by ELISA [16-18].

Results: Expression and purification of the LFD1 AND PAD4 proteins Selected colonies were cultured in a LB medium at 37 °C, after reaching logarithmic growth, the expression induced by 1 mM IPTG at final concentration. The expression and quality was evaluated by 12% SDS-PAGE gel .The LFD1and PAD4 protein band was indicated at 33 and 28 kDa respectively.(Fig.1,2). Encapsulation of mixed proteins and chracterization The results of PEG-PLA nanoparticles loaded with mixed proteins LFD1 and PAD4 (separately) by DLS are shown in the table1 and diagram1. Evaluation of antibody titration against recombinant protein by indirect ELISA An indirect ELISA was used to analyze the antibody titration and to characterize its ability to detect antigens in each injection phase. Blood samples were randomly taken from test and control mice, one week after the second, third, and fourth injection with LFD1-PA4 (fusion) and LFD1 + PA4 (mixed) proteins. After serum isolation, ELISA was performed. The antibody titration is shown in Diagrams 2. Figure (1) Purification of LFD1 protein from Ni column: Column 1) Before Ni column, column 2) Sample containing proteins (Flow) collected from Ni column Column 3) Buffer C collected, Column 4) Buffer D collected, Column 5) Collected buffer E, Column 6) Protein marker Column 7) Collected MES buffer. Figure (2) Purification of PAD4 protein from Ni column: Column 1) Before Ni column, Column 2) Sample containing proteins (Flow) collected from Ni column Column 3) Buffer D collected, Column 4) Buffer E aggregate ¬ Collected, columns 5 and 6) Collected MES buffer, column 8) Protein marker. Table (1) Investigation of physicochemical properties of nanoparticles using dynamic light diffraction پتانسیل زتا (میلی ولت) اندازه (نانومتر)PDI CONTROL -32.1 13.88 0.337 ENCAPSULATED -27.7 109 0.394 Diagram 1- PEG-PLA nanoparticle size distribution range containing LFD1 + PAD4 mixed protein under optimal conditions by DLS. Diagrams 2-ELISA curve of IgG antibody production after each injection of mixed protein LFD1 and PAD4 in three forms of free (A), loaded one injection (B) and loaded two injections (C) against LFD1-PA4 protein (curves are shown in the picture box).

Conclusion: In this study, we evaluate the antibody titer produced by injecting mixed proteins (LFD1 and PAD4) in three forms: free (four injections), loaded (once injected) and loaded (twice injected) and calculate its amount in each injection showed that the highest antibody titer against nanoparticles loaded with mixed antigen. Most researchers are currently working on vaccines based on recombinant protective antigen (rPA) for anthrax(19-22). The triple nature of anthrax toxin raises the expectation that other parts of the toxin, such as lethal factor and PA, will also be involved in the production of toxin-neutralizing antibodies. Various studies have shown that concomitant administration of lethal factor and PA increases the level of antibodies against PA in mice, and this effect of lethal anticoagulant adjuvant is related to its amino terminus, LFD1. This region has been used by researchers to transmit various antigens and has been shown to elicit immune responses to CD4 + and CD8 + T cells [23-24,26]. Based on the findings of this study, it can be concluded that encapsulation of combination of region 1 of lethal factor (LFD1) and region 4 of protective antigen (PAD4) in PEG-PLA diblock copolymer nanospheres can be a good candidate for anthrax vaccine.

Keywords: Bacillus anthracis. protective ag , lethal factor,polymeric nanoparticles,

Evaluation of anticonvulsant activity of 2-aryl-3-triazolylindole derivatives in mice (Research Paper)

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Introduction: Epilepsy is a common disorder in the central nervous system. Almost one percent of the world's population suffers from seizures. Epilepsy is a disorder with a complicated nature that various factors play roles in it. Pharmacotherapy with new antiepileptic drugs (AEDs) is the first way to treat epilepsy. In 70% of patients, their seizure is controlled by taking one to three AEDs, about 60% of patients experience adverse effects and 33% of patients have to change their drugs. Side effects and teratogenicity of newer AEDs have made them more commonly used in the treatment of resistant epilepsy. Given the importance of discovering new AEDs with better efficacy and fewer side effects, this study with the purpose of evaluating the anticonvulsant effects of new triazolylindole derivatives, which differ in their substituents on benzene and indole rings, was done by PTZ and MES methods.

Methods: Male NMRI mices (20-25g, n=4 heads) were selected. The compounds were injected intraperitoneally (IP) to each animal group in both MES and PTZ methods at doses of 30 and 100 mg/kg. In the PTZ method, 0.5 hour after the injection of the compounds, PTZ was injected intraperitoneally at a dose of 100 mg/kg, and the animals were observed for 0.5 hour and deaths from tonic-colonic seizures were recorded. In the MES method, 0.5 hour and 4 hours after the injection of the compounds, the animal was stimulated by an electrical current stimulator (f: 60 Hz, I: 50 mA, T: 0.2 sec) through the ear electrodes and the occurrence or absence of seizures incidentally Hind Limb Tonic Extension (HLTE) was recorded as the response. Also in both methods, a group as a positive control received standard drug (diazepam, 2 mg/kg) and a group as a negative control received solvent (DMSO, 5 ml/kg).

Results: Among the compounds studied, none of them had a protective effect on the PTZ method. In the MES method, at a dose of 100 mg/kg, compounds containing fluorine substituents at para- and ortho positions of the benzene ring and fluorine substituent at position 5 of indole ring (compound A), chlorine substituents at the para- and ortho positions of the benzene ring and chlorine substituent at

position 7 of indole ring (compound B), and fluorine substituent at the para position of the benzene ring and chlorine at position 5 of indole ring (compound C), had the highest protective effect (50%) at 0.5 h after injection and compounds containing fluorine substituents at para- and ortho positions of the benzene ring and chlorine substituent at position 7 or 5 of indole ring (compounds D and E), had the highest protective effect (50%) at 4 hours after injection. At a dose of 30 mg/kg, compounds containing chlorine substituents at para- and ortho positions of the benzene ring and fluorine substituent at position 5 of indole ring (compound F), and compound C had the highest protective effect (25%) at 0.5 h after injection, and compounds C and E had the highest protective effects (25%) at 4 hours after injection.

Conclusion: Generally, the compounds studied had moderate anticonvulsant effects. The studied compounds showed the highest anticonvulsant activity in the MES method and were not effective in the PTZ method. Since the model of MES in animals is a measure of the effectiveness of the drug in generalized tonic-colonic epilepsy in humans, therefore, these compounds have the potential for further studies and more detailed evaluations to determine the exact mechanism of action by docking and molecular modeling studies, as well as toxicity tests to calculate LD50 and Rota-rod test to evaluating neurotoxicity. The results also indicate that the type and position of substituents of the indole ring are more effective than substituents of a benzene ring on the compound's anticonvulsant effects.

Keywords: Epilepsy, Pentylentetrazole, Maximal electroshock seizure, Triazole, Indole

Evaluation of antioxidant and anticancer activity of methanolic extract of Prangos crossoptera. (Research Paper)

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Introduction: Medicinal plants are sources of natural active compounds that can be used to prevent and treat diseases. Prangos genus is one of the most important medicinal plants. The members of the Prangos genus have been widely used in the Iranian traditional medicine for different purposes. This genus consists of about 30 species. In Iran 15 species are present, among which five are endemic. Prangos crossoptera with the common Persian name of "Jashir-e-Zagrosy" is a perennial plant from Apiaceae family which is endemic to Iran. According to the literature, biological properties of Prangos crossoptera have already been the subject of a few investigations. The aim of this study was to evaluate the antioxidant and anticancer activity of methanolic extract of Prangos crossoptera.

Methods: In the current study, the plant samples were collected from Kurdistan province in Iran. For preparing the methanolic extract, 10 mg of powdered shade-dried plant were macerated with methanol (1:10) three times. The antioxidant potential of the plant extract was evaluated by DPPH (2, 2-diphenylpicrylhydrazyl) assay with reference to a synthetic antioxidant, butylated hydroxytoluene (BHT). Anticancer activity of the methanolic extract was examined on human breast cancer cell line (MCF-7) using [3-(4, 5-dimethylthiazolyl)-2, 5-diphenyl-tetrazolium bromide (MTT) method.

Results: The DPPH assay showed that the methanolic extract of studied plant had significant antioxidant effect and could scavenge free radicals with IC50 value of 0.1 mg/ml. Moreover, this assay indicated that methanolic extract had higher antioxidant activity compared with BHT as a synthetic standard antioxidant (with IC50 value of 0.13 mg/ml). Evaluation of anticancer effect of extract showed that the viability of MCF-7 cells was inhibited in a time and dose- dependent manner. MTT assay indicated that different concentrations of the extract reduced the viability of MCF-7 cells after 4, 8 and 24h of incubation, with IC50 values of 0.87, 0.51 and 0.24 mg/mL, respectively. A 100% cytotoxicity was observed in concentrations higher than 1mg/mL.

Conclusion: The obtained results showed that Prangos crossoptera had a significant antioxidant effect and a high reducing power. On the other hand, this plant played an acceptable anticancer role. Therefore, Prangos crossoptera can be used as effective sources to develop anticancer drugs. It is recommended to determine the important components of this plant and assess their anticancer mechanisms.

Keywords: Prangos crossoptera, anticancer effect, antioxidant effect

evaluation of Beta-Tricalcium phosphate /polycaprolactone nano composite scaffold in bone regeneration application (Research Paper)

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Introduction: The aim of bone tissue engineering is to facilitate the healing of the damaged tissue and restores the function sustainably and by using different nanocomposite it has been trying to design a biocompatible and biodegradable scaffold with optimal properties for bone regeneration.

Methods: In this study different amounts of BTCP (beta-tricalcium phosphate) a precursor of bone mineral phase was composited with polycaprolactone, to enhance biological and mechanical properties of scaffolds. BTCP-PCL composites with the 0, 10, 20, and 50 weight percent (WT%) were prepared by particulate leaching method using sodium chloride as porogen and freeze-drying method) lyophilization (. The scaffold architecture consists of relatively large interconnected pores modeled after porogen and smaller pore resulting from the freeze-drying process. Material properties of scaffolds like XRD, SEM micrographs of scaffolds, and EDAX analyses were characterized. mechanical properties of the nanocomposite scaffolds were characterized by the compression strength test and the bioactivity of the scaffolds in simulated body fluid (SBF) was assessed. The proliferation, cell attachment, and differentiation of mouse bone marrow-derived mesenchymal stem cells (BMSCs) on the scaffolds were analyzed by scanning electron microscopy (SEM), live-dead, Alizarin red, and alkaline phosphatase assays.

Results: The results showed that the addition of BTCP to the PCL matrix improved the properties of scaffold and it indicated that BMSCs can attach firmly on the scaffolds and by increasing BTCP the amounts of HA produced were significantly elevated. Moreover, no toxicity was reported after 1, 3, and 5 days after cell seeding on scaffolds and alkaline phosphatase activity demonstrated enhanced proliferation and differentiation of cells on scaffolds containing nanoparticles in comparison with pure PCL.

Conclusion: It is concluded that BTCP-PCL nanocomposites with the optimum concentration can be a good candidate for bone tissue engineering applications.

Keywords: Polycaprolactone, porous nanocomposites, freeze-drying, microsphere, Bone Tissue Engineering

Evaluation of changes in hepatic tissue , enzymes and inflammation cytokines due to experimental common bile duct obstruction in rat model (Research Paper)

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2.

Introduction: There is controversy among clinicians for diagnostic bile duct obstruction. The primary aim of this study was to examine the histopathological changes of the liver and the level of inflammatory factors (TNF-α), Tumor necrosis Factor-α, and Interleukin-6 (IL-6) during the obstruction. The secondary goal of this study was to examine the liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bile acids (TBA), and gamma-glutamyl transferase (GGT).

Methods: Consequently, we purchased thirty-five rats. The rats were housed for two weeks to adapt to the new conditions. We randomly placed these animals into three groups. The first control group (control-1) with five rats, the second control group (control-2) with fifteen rats, and the case group with fifteen rats. Both control-2 and case groups received ketamine, xylazine, and isoflurane to induce anesthesia. Although, abdomens of the rats in control-2 were knifed, but the bile duct obstruction was not induced. In spite, the abdomens in the case group lacerate and portal layers of the main bile ducts were chocked by using silk sutures. Hepatic tissue and serum of the rats in all the three groups were analyzed every two days. Hematoxylin/Eosin followed by microscopic observation were applied to study the liver tissues. Also, the biochemical analysis of the serum sample was done using an auto-analyzer.

Results: Our results revealed a steady increase in levels of TBA, TNF-α, and IL-6 during the bile duct clog. In spite, we could not see any significant changes in the liver enzymes such as AST, GGT, and ALT in the case group, in comparison to both control groups. Histopathology tests reveal inflammatory cells around the portal area in liver tissues. Besides, necrosis and ballooning have been seen around the portal area

Conclusion: . Thus, rising the liver enzyme such as TBA in addition to inflammatory factors such as TNF-α and IL-6 can be employed to diagnose the biliary duct obstruction in the first weeks

Keywords: Key words: Bile duct obstruction, Bile duct inflammation, Liver enzymes, Steatosis, TNF-α, IL-6

Evaluation of Chlorpyrifos insecticide on the organogenesis stage in Mus musculus (Research Paper)

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Introduction: Nowadays, one of the issues that matter in infertility is abortion or teratogenicity of embryos, followed by environmental pollution. Additionally, the continuous use of pesticides as the requirements of modern agriculture can increase the number of released radicals, which ultimately affects cell membranes and cell death via apoptosis pathway

Methods: In present study, 30 heads NMRI mice were divided into 3 groups: 1) Chlorpyrifos received group, 2) DMSO received as the sham group, 3) Control group. The mice were mated and euthanized 10 days post gestation. The number of embryos, progesterone and estradiol hormones and the liver enzymes levels of mouse mothers were evaluated in each group. The apoptosis pathway genes (Bax and Bcl2) and protein expressions (caspase3 and caspase9) were evaluated in the embryos of each group by qPCR and immunohistochemistry staining, respectively

Results: The number of embryos in the experimental group was significantly lower than from the other groups. The liver enzymes and hormone levels were higher in CPF induced mice in comparison to the others. The mRNA expression of Bax in the embryos was significantly higher in the CPF group compared to sham and control groups. Caspase3 and Caspase9 protein expression revealed a higher rate of apoptosis in CPF group embryos.

Conclusion: Continuous use of Chlorpyrifos can be regarded as having a negative effect on pregnancy as well as raising the mechanism of apoptosis in the development of embryos that may contribute to abortion or the birth of teratogenic disorders embryos

Keywords: Chlorpyrifos, Embryos, Apoptosis pathway, Mice

Evaluation of cytotoxic effect of different Iranian Chrysanthemum morifolium cultivars against MCF7 cell lines (Research Paper)

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Introduction: Cancer is the second leading cause of death in the world (Khakdan and Piri, 2013). Breast cancer is the most common disease in women, which can be treated with natural therapy (Cushman & Nagarathnam, 1991). Despite the availability of synthetic drugs, plants still are one of the important sources for modern drug development for anticancer activity (Kashif et al., 2014), as over 50% of anticancer drugs used in therapical trials were isolated from natural sources or are related to them . The medicinal value of plants depends on some phytochemicals (Khakdan and Piri, 2013) like terpenes, phenolics, and alkaloids that produce a physiological action on the human body (Dai & Mumper, 2010: Kashif et al., 2014). Chrysanthemum morifolium has been used as an herbal in traditional medicine applications for several years. Recently, it had been reported that Chrysanthemum flavonoids showed cytotoxic effect against human breast cancer cells (Liu, Mou, Zhou, Zhou & Shou, 2018). In Iran, despite the widespread ornamental use of these herbal plants, no scientific assessment has been reported for anticancer effect of them. considering the anti-cancer effect of this plant, this research was conducted to investigate cytotoxic and growth inhibitory activities of C. morifolium flower extract on human breast cancer cell lines (MCF7).

Methods: Sixteen cultivars of Chrysanthemum (Chrysanthemum morifolium Ramat.) including Shokoh, Atashgoon, Atash2, Sahar, Marmar, Sahand2, Dorna2, Ashna, Hour, Erica, Poya3, Bolor, Romina, Farhood, Taraneh, and Mehrnoosh2 originated from the Iranian Research Center for Ornamental Plants, Mahallat, Iran were used in this study. Dried ground flowers (2.5 g) was extracted with methanol-water (50ml, 80:20, v/v) and orbital shaker for 24 h. The extract was filtered through three layers of cheesecloth. The filtered extracts were evaporated under reduced pressure to obtain dried residue and after that a stock solution was prepared by dissolving the extract powders in DMSO to form a concentration of 100 mg/ml. Human cancer cell lines (line MCF7) were cultured in RPMI-1640 media. Three wells for each concentration were seeded. Cells were maintained in a humidified 5% CO2 incubator at 37 °C. The effect of Chrysanthmeum extracts on MCF7 cells were determined by 3-(4,5 dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide (MTT) assay. Cell viability was calculated using the following formula: % Cells viability= (OD sample/OD control) ×100. The data represent mean ± SE from triplicate experiments. One-way analysis of variance (ANOVA) was carried out and Fisher's (protected) least significant difference (LSD) was applied to compare means at the 95% confidence level using SAS ver. 9 software.

Results: The results demonstrated that all tested extracts exhibited different potency of cytotoxic activity against the MCF7 cell lines at five various concentrations. All cultivars showed maximum cytotoxic effect at 0.312 mg/ml

concentration which the methanol extracts of cultivars “Dorna2” and “Farhood” inhibited the viability of the cancer cell lines by up to 50%. Murayama et al. (2012) reported that both leaf and flower water extracts of Chrysanthemum suppressed the proliferation of MCF7 cell lines in a dose dependent manner at concentrations >25 µg/ml. Lee et al. (2014) evaluated anticancer activity of some Korean Chrysanthemum sp. (C. boreale, C. indicum and C. morifoium). These methanolic extracts exhibited relatively potent inhibition at a concentration of 200 µg/ml against MCF7 cell lines with cell viability of 47-63%. Treatment (200 µg/ml) of C. morifoium suppressed 49% of cell viability in this study. Flavonoids have been found to possess anti-cancer activity due to their impact on the transduction in cell proliferation (Khakdan & Piri, 2013). Previous studies reported that the flavonoids from C. morifolium exhibited significant cytotoxicities against human breast, liver and colon cancer cells (Peng, Zou & Xu, 2010; Xie, Yuan, Yang, Wang & Wu, 2009). So, the observed anti-cancer effect of the extracts on the MCF7 cell lines could be attributed to the presence of these bioactive compounds.

Conclusion: The results demonstrated that different Chrysanthemum cultivars could be evaluated as an anticancer agent in different concentrations, which is useful in the cytotoxic evaluation of new herbal drugs. The present study established that the Iranian Chrysanthemum cultivars can be considered as promising sources of anti-cancer agent.

Keywords: Chrysanthemum, Breast cancer, MCF7, Toxicity, Herbal drug

Evaluation of GAS5 and MEG3 LncRNAs Expression Changes in Patients with Gastric Cancer (Research Paper)

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Introduction: Gastric cancer is the second leading cause of cancer death. Gastric cancer is characterized by a growth of cancerous cells within the lining of the stomach. This type of cancer is difficult to diagnose because most people typically don't show symptoms in the earlier stages. Gastric cancer is directly linked to tumors in the stomach. However, some factors might increase the risk of developing these cancerous cells. These risk factors include certain diseases and conditions, such as H. pylori bacterial infections, tumors in other parts of the digestive system, Stomach lymphoma, stomach polyps, smoking, Geography, and Diet. Gastric carcinogenesis is an elaborate multistep process involving genetic dysregulation of proto-oncogenes and tumor suppressor genes and has recently entered the era of Long non-coding RNAs (lncRNAs), a group of transcripts that modulate many cellular functions. With a total length of > 200 nucleotides, they regulate the expression of genes through chromatin remodeling and transcriptional and post-transcriptional alterations. Aberrant expression of lncRNAs in various human malignancies has implied their role in the pathogenesis of cancer. Long non-coding RNAs (lncRNAs) as regulators of gene expressions at different genomic, transcriptomic, and post-transcriptomic levels are among putative biomarkers and therapeutic targets in gastric cancer.

Methods: In this study, 40 tissue (including 25 gastric cancer tissue and 15 control tissue) were obtained from patients with a definite diagnosis of gastric cancer by specialists and pathologists, and people referred to "Shahid Ghazi Tabatabaie Hospitals of Tabriz, Iran". RNA was extracted from tissue samples, and cDNA was synthesized from RNA. Real-time PCR was used to determine the lncRNAs (GAS5, MEG3) gene expression in gastric cancer patients. The samples were taken after the acquisition of a written consent form signed by all the patients. Statistical calculation of data was done by applying the SPSS software. A p-value of <0.05 was considered significant.

Results: Our findings revealed that the lncRNA GAS5 and lncRNA MEG3 expression level was significantly decreased in gastric cancer tissue compared with healthy tissue.

Conclusion: Investigating the expression level changes of these lncRNAs provides novel and exciting possibilities for mastering the treatment of gastric cancer.

Keywords: Long non-coding RNA; Stomach; Gastric; GAS5; MEG3

Evaluation of general health of caregivers of patients with mental disorders referred to psychiatric center in Zahedan (Research Paper)

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Introduction: Mental illness is one of the leading causes of disability and affects the performance of life and family in social, family and educational dimensions. Therefore, chronic medical complications not only affect the life of the sufferer but also various aspects of life. The family also changes their health, including their health. The aim of this study was to determine the general health of caregivers of patients with mental disorders and related factors.

Methods: This is a descriptive-analytical study. The number of samples was 307 people who entered the study by available sampling method. In this study, 28-item background information and general health questionnaire was used. Descriptive and inferential statistics (Chi-square test and Spearman correlation coefficient) were used to analyze the data.

Results: The level of general health of 46.6% of caregivers was favorable, 46.6% was somewhat favorable and 6.8% was unfavorable. There was a significant relationship between caregivers' general health and family economic status (P = 0.001). There was also a significant relationship between caregivers 'general health and caregivers' education level (P = 0.033).

Conclusion: The family factor is one of the psychosocial factors that affects the clinical course of the disease and the outcome of the disease, including recurrence. And there is a close relationship between how the family communicates and the rate of disease recurrence. Therefore, nurses need to pay serious attention to the family (the main social unit)

Keywords: Mental Disorders, General Health, Caregivers

Evaluation of Immobilized- Metal Affinity Chromatography (IMAC) for host cell proteins (HCPs) removal from anti-HER2 scFv expressed in E.coli (Research Paper)

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Introduction: Host cell proteins (HCPs) are process-related impurities derived from the host organisms and are unrelated to the intended recombinant product. HCPs have potential effects on biological activity, immunogenicity, and consequently product safety and efficacy. To produce safe and efficient protein biopharmaceuticals, HCPs should effectively be removed by chromatographic steps in downstream purification process. Therefore, monitoring the removal of HCPs in final drug product to acceptable amounts (<100 ppm) is a regulatory requirement. In this study, we aimed to evaluate the efficacy of purification process using Immobilized- Metal Affinity Chromatography (IMAC) for separation of HCPs from the recombinant anti- HER2 single chain fragment variable (scFv) expressed in Escherichia coli. In scFv, the variable regions of heavy (VH) and light (VL) chains of an antibody are connected with each other by a flexible peptide linker. scFvs display improved pharmacokinetic properties, such as better tissue penetration and rapid blood clearance while having specific affinity and low immunogenicity. Anti-HER2 scFv can be fused to the marker proteins, toxins, radioactive agents and drugs and can be used for treatment and diagnosis of HER2+ breast cancer which is the most common cancer and the first cause of cancer death in women, worldwide

Methods: Anti- HER2 scFv was expressed in BL21 (DE3). Anti- HER2 scFv protein was purified by IMAC using Ni-NTA resin under native, denaturing and hybrid conditions. Purity of samples was investigated by SDS-PAGE. Total protein concentration of samples was measured by BCA assay. Herein, a commercial sandwich Enzyme-Linked Immunosorbent Assay (ELISA) (E.coli HCP ELISA kit) was used to determine HCP concentration of different samples.

Results: The yield and purity of anti-HER2 scFv purified under hybrid condition was higher than those purified under native and denaturing methods. The ELISA result showed that all of three methods caused reduction in HCP concentration of elute samples compared with wash and flow through samples. Furthermore, the lowest concentration of HCP in elute samples was obtained by IMAC purification under hybrid condition (~2-3 ng/mL).

Conclusion: : IMAC under hybrid condition was a suitable method for separation of HCPs from the recombinant anti-HER2 scFv expressed in BL21 (DE3).

Keywords: Anti-HER2 scFv, HCP, Purification, IMAC

Evaluation of Mutations in 23S rRNA genes of Helicobacter pylori in Paraffin-Embedded Gastric Biopsy Specimens from Iranian Gastric Cancer and Gastritis Patients (Research Paper)

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Introduction: Helicobacter pylori (H. pylori) infection is considered as one of the main causes of gastric cancer. Treatment failure of the infection often occurs due to antibiotic resistance. Herein, we aimed to evaluate the mutations in 23S rRNA gene of H. pylori which are associated with clarithromycin resistance, in paraffin-embedded gastric biopsies from patients with gastric adenocarcinoma and gastritis in Tabriz, the northwest of Iran.

Methods: In the study, 80 paraffin-embedded tissue sections from 40 gastric cancer and 40 gastritis patients in the Imam Reza hospital, Tabriz, Iran were collected. The existence of ureC gene was verified by PCR method. Genotypical clarithromycin resistance was investigated by Real time PCR method and determination of the melting temperature

Results: The results of ureC amplification showed that DNA of H. pylori was present in the 82.66% of the obtained DNA samples. About 45.16% of samples were resistant to the clarithromycin. Based on the results from Real time PCR, the frequency of mutations was as follow A2143G 64.28%, A2142G 44.44% and A2142C 1.11%.

Conclusion: A2143G mutation is the most frequent mutation among clarithromycin resistant genes in Iran. Screening for this mutation could help researchers to investigate the most effective anti-H. pylori antibiotics and to prevent antibiotic resistance.

Keywords: Gastric cancer, H. pylori, clarithromycin resistance

Evaluation of Mutations in rdxA and frxA genes of Helicobacter pylori in Paraffin-Embedded Gastric Biopsy Specimens from Iranian Gastric Cancer and Gastritis Patients (Research Paper)

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Introduction: Helicobacter pylori (H. pylori) infection is considered as one of the main causes of gastric cancer. Treatment failure of the infection often occurs due to antibiotic resistance. Herein, we aimed to evaluate the mutations in rdxA and frxA genes of H. pylori which may be associated with metronidazole resistance, in paraffin-embedded gastric biopsies from patients with gastric adenocarcinoma and gastritis in Tabriz, the northwest of Iran

Methods: In the study, 80 paraffin-embedded tissue sections from 40 gastric cancer and 40 gastritis patients in the Imam Reza hospital, Tabriz, Iran were collected. The existence of ureC gene was verified by PCR method. PCR reaction and sequencing were used for the evaluation of mutations in rdxA and frxA genes.

Results: The results of ureC amplification showed that DNA of H. pylori was present in the 82.66% of the obtained DNA samples. About 53.22% of samples were resistant to the metronidazole. The mutations of rdxA gene were 66.66% missense, 30.30% frameshift and 3.03% non-sense. The mutations of frxA gene were 36.36% missense, 54.54% frameshift and non-sense 9.09%.

Conclusion: missense and frameshift mutations are frequent in rdxA and frxA genes. Screening for these mutations could help researchers to investigate the most effective anti-H. pylori antibiotics and to prevent antibiotic resistance.

Keywords: Gastric cancer, H. pylori, metronidazole resistance

Evaluation of nano-lipid system containing curcumin extract against E.coli and S. aureus by Mozaffari method (Research Paper)

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Introduction: The aim of this study was to characterize the nano-lipid system containing curcumin extract against E.coli and S.aureus. For this purpose, a lipid system containing curcumin extract has been developed by Muzaffari method.

Methods: The type of study is laboratory research. This nanoparticle is made by Mozaffari method. Particle characterization has been performed in terms of size and charge with DLS and morphology with the Atomic Energy Microscope (AFM) and the amount of loading and release with the spectrophotometer. MIC and MBC tests were then studied to evaluate the performance of nanoparticles containing curcumin extract on E.coli and S.aureus.

Results: The average particle diameter was about 57 nm and its zeta potential was -15.6 mV. The loading rate in nanoparticles was 92.6%, which was calculated by reading the absorption of light from the standard curcumin curve. In addition, minimum inhibitory concentration (MIC) of nanoparticles of E.coli and S.aureus was 15.625 and 31.25 mg / ml and minimum bactericidal concentration (MBC) of E.coli and S.aureus was 31.25 and 31.25 mg / ml.

Conclusion: nano-lipid system containing curcumin extract kill gram-positive (Staphylococcus aureus) and gram-negative bacteria (E.coli) and can be used as antibacterial nano-systems.

Keywords: E.coli, Staphylococcus aureus, Curcumin, Nano particle.

Evaluation of nosocomial infections among patients admitted to Bahrami Children's Hospital in the spring of 1398 (Research Paper)

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Introduction: Nosocomial infections are one of the most important health issues in the world, in which we must pay special attention to pediatric infections to prevent antibiotic resistance in the future. The high cost of treatment, as well as the large number of patients, their mortality and the increasing number of these infections, highlight the need for special attention and effective measures to prevent nosocomial infections.

Methods: This is a descriptive-analytical study among 2900 patients admitted to Bahrami Children's Hospital in the first quarter of 1398. The data were completed with the help of the hospital's microbiology department.

Results: The data showed that the prevalence of infection in the study population was 4.8%. The most common infections were urinary tract infections, blood cultures, throat and tracheal, that infection rate is 69.28%, 14%, 8% and 8.72%, respectively. The most common causes of infections are E.coli, klebsiella pneumoniae, Enterobacteriaceae, Staphylococcus aureus, Pseudomonas and Streptococcus, respectively.

Conclusion: According to the results of this study, the prevalence of nosocomial infections in this study is consistent with statistics from other studies. Therefore, adhering to hygienic principles and some recommended items for each patient to control and prevent nosocomial infections is emphasized. These principles include: timely use of medical interventions, hand washing, health education, continuous monitoring of officials, proper use of disposable devices, controlled use of antibiotics and proper care of surgical wounds.

Keywords: Nosocomial infections, pediatric infections, urinary tract infections, blood cultures infections

Evaluation of pathogenicity, characteristics, mode of transmission, and host association of some important Helicobacter species (Review)

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Introduction: Recently, the genus Helicobacter includes 54 identified species. This genus can be divided into two major groups, comprising gastric and enterohepatic species. Specifically, the gastric Helicobacter species can survive in the acidic environment of stomach. However, the enterohepatic Helicobacter species can survive in the mucosal surface of intestinal tract and liver. This review article generally aimed to discuss and describe the biology and pathogenesis of two critically important Helicobacter species, including Helicobacter pylori, as a gastric species, and Helicobacter pullorum, as an enterohepatic species, in humans and animals.

Methods: H. pylori, first being discovered in 1982 from human, has been categorized as a class 1 carcinogen by the International Agency for Research on Cancer (IARC). Notably, epidemiological studies have exhibited that almost 50 per cent of the population are infected by this zoonotic pathogen worldwide. But, just a portion of infected individuals have been implicated in a wide spectrum of gastric disorders that can lead to Peptic Ulcer Disease (PUD) or Gastric Cancer (GC). In Iran, for instance, it has been estimated that more than 90% of population does seem to be infected with this gram negative species. In developing countries, H. pylori infection mainly occurs in childhood and infected people may carry this bacterium in their stomach for lifelong. Obviously, there have been several risk factors being associated with the transmission of H. pylori to humans, namely consumption of uncooked milk, vegetables, and meats, the presence of domestic animals, the presence of rodents near or in the houses, the contact with pets, and so on.

Results: H.pullorum, first being discovered in 1994 from intestinal contents of chicken and laying hens, has been taken into account as an emerging foodborne human pathogen which can pose a perilous risk to public health. Most of the poultry, such as chicken, turkey, laying hen, human, meat, and even water could be said as a source of contamination for this gram negative bacterium. Importantly, the fact that the Iranian poultry industry has become the first in the Middle East and 7th throughout the world by producing 2 million metric tons of chicken meat, has given importance to this life-threatening pathogen. There have been some significant human diseases being linked to this non-spore forming bacterium, namely gastroenteritis, inflammatory bowel disease, hepatobiliary disease, Crohn, s disease, and so on.

Conclusion: To sum up, in this review article we attempted to reveal the lifestyle of two significant Helicobacter species, including H. pylori and H. pullorum. In fact, considering these foodborne pathogens would be of utmost importance and therefore more elaborate studies are needed to discuss about the mentioned pathogens.

Keywords: review article, Helicobacter pylori, Helicobacter pullorum, pathogenicity

Evaluation of probiotic potential of yeast isolated from traditional cheese manufactured in Ardabil (Research Paper)

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Introduction: As the food industry continues developing new products and processes, consumers are focused on food safety, diet and health aspects of their food. Yeasts are important microorganisms in the fermentation of foods and beverages, and some yeasts have been used as biocontrol agents and novel probiotics. During the last decades, since they have shown numerous beneficial effects on human health, their usage as probiotics has been increasing. Probiotics are desirable and natural tools for providing balance to the intestinal microflora. They are consumed either as food or non-food preparations. New species of probiotics are constantly being identified. In this study, isolation, characterization, and identification of yeast strains from natural sources and retail cultures were investigated. Some probiotic properties of the isolates were determined.

Methods: Samples were collected from traditional cheeses. The samples were cultured in the YGC agar medium by pour plate method Then, differentiation between yeast isolates was performed by CHOROM agar media and molecular identification of the isolated isolates was performed by PCR and sequencing of PCR products. All isolates were also investigated for their ability to grow in SD broth at different temperatures, at different pH, and different levels of added ox bile. The yeast isolates were tested for antimicrobial drug sensitivity against antifungal agents were placed on yeast inoculated YGC medium plates. The antagonistic properties of isolated yeast species were determined by modifying the disc diffusion method.

Results: A Set of five isolates were isolated from four locales during three periods of sampling and after the preparation of three serial dilutions, they were cultured on YGC agar. Biochemical and morphological analyses were accurately performed for all five isolates .four isolates were positive urea. Three isolates weren't able to ferment arabinose sugar and grow at 45 ° C. Genetic identification was used for the one isolate, SH04, which was similar to saccharomyces boulardii species respectively. All isolates, especially SH04 isolate, were able to grow at different pH and salts. All isolates have had probiotic properties.

Conclusion: Probiotics play a critical and vital role in human nutrition. In recent years, new strain isolation, characterization and verification of potential health benefits particularly related to probiotic traits have been a very attractive area for researchers. Probiotic properties are strain-specific, therefore new strains must be

well characterized. The results indicated that this yeast showed notable potential probiotic properties.

Keywords: Yeast, Isolation, probiotic

Evaluation of Role of Herpes Simplex Virus 1-2 and Cytomegalovirus in Alzheimer's Disease (Research Paper)

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Introduction: Alzheimer's disease (AD) was diagnosed over 100 years ago though Alois Alzheimer. Studies reported the pathological signs devastating disease. Different environmental factors, such as infection have cause AD. Herpes Simplex virus type 1 (HSV1), type 2 (HSV2) and Cytomegalovirus (CMV) are related to AD in different studies.

Methods: To explore whether carriage of HSV1, HSV2 and CMV, developed the risk of progressing AD, which may prevent and can be used for the treatment of AD. Plasma samples were isolated from 100 AD patient in aseptic conditions (47 women and 53 men). Viral DNA was then isolated for PCR methods. Quantitative and qualitative evaluation of extracted DNA were performed by Spectrophotometry and electrophoresis on Agarose gel. Three pairs of primers were used for each virus. The variables and the data were then analyzed by SPSS software.

Results: The results showed that the prevalence's of CMV, HSV-1 and HSV-2 were 27%, 8% and 4%, respectively. Although CMV in AD patients was most prevalence, but HSV1 and HSV2 were found in patients with advanced AD. Also, the HSV1 and HSV2 prevalence's were significantly associated with dysphoria, hallucination, insomnia and depression ($P<0.05$), while CMV prevalence was significantly associated with hallucination and dysphoria ($P=0.001$). AD symptoms were higher in patients with HSV1 and HSV2. Seemingly, HSV is related to the severity of AD. Patients with diseases such as, diabetes, hypertension, and Dyslipidemia likely develop CMV.

Conclusion: These results suggest that CMV infection is associated to increased risk of AD and a quick rate of cognitive decline in elderly populations. The prevalence of these viruses in AD is more pronounced rather than other studies.

Keywords: Alzheimer's, Herpes Viruses, Frequency, Cytomegalovirus

Evaluation of the difference in the effectiveness of adipose stem cells (ASCs) with conditioned media (CM) in the treatment of atrophic acne scars with two methods (fractional carbon dioxide laser and microneedling) (Research Paper)

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Introduction: It is a challenge to treat acne scars and a multimodal combination approach is necessary. While fractional CO2 lasers (FCLs) and microneedling are an established treatment options, the role of the adipose stem cells (ASCs) with conditioned media (CM) in the treatment of atrophic acne scars is not established. We combined the two methods to assess the proposed synergistic action on atrophic acne scars.

Methods: We included thirty patients in our study, which separated by two groups (15= FCLs+ADSC-CM) and (15= microneedling+ADSC-CM). The age of the patients varied from 24 to 40 years. The first group was treated with FCLs+ADSC-CM and the second group was treated with microneedling+ADSC-CM .Treatment sessions were performed in 4 sessions with an interval of 21 days. Before treatment, biometric indices of patients' facial skin in areas with atrophic acne scars were measured and recorded as evaluation in each session.

Results: Symptoms of redness, edema, and pain were significantly less in areas treated with Microneedling + ADSC-CM compared with FCLs + ADSC-CM. Injury and inflammation associated with laser treatment are significantly reduced due to the use of ADSC-CM. Both methods were effective in management of acne scars. The final assessment took place at 6 months. Combined microneedling + ADSC-CM-treated areas had a significantly better response ($p = 0.01$)

Conclusion: As a result, our findings show that both methods are effective in reducing scars. microneedling and conditioned media as a combination method is an effective and safe method in the treatment of atrophic acne scars. In this method, compared to the use of laser, there is a slight pain experience and low complication rate in patients with acne scars. And this satisfaction is higher in patients with dark skin.

Keywords: Atrophic acne scars , Microneedling , Stem cell , Fractional CO2 lasers, ADSC-CM

Evaluation of the effect of anesthesia on the mother and the fetus in selective cesarean section (Review)

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Introduction: Cesarean section was one of the most common surgeries in the world and it still is. It is not possible without general or local anesthesia. One of the most important issues among anesthesiologists, gynecologists and pediatricians is the type or method of anesthesia used in cesarean section. For this surgery, general anesthesia or local anesthesia can be used. The local method can be done either epidural or spinal. The use of spinal anesthesia is more common. The choice of the type of anesthesia depends on factors such as the cause of the surgery, the emergency, or the selectivity and desire of the mother. Therefore, mothers must have almost complete information about their complications in order to choose the right method of anesthesia in selective cesarean section. Thus, the present study was performed to determine the effect of anesthesia on mother and fetus in elective cesarean section.

Methods: This study is a review that was done during the period (2020-2000), by searching in valid foreign databases like Pubmed, google scholar, Scopus, with English keywords such as “Analgesic methods”, “Cesarean section”, “complications of anesthesia” and “mother and fetus”, And in valid internal databases with Persian keywords like “عوارض بیهوشی”, “سزارین”, “روشهای بی دردی” and “مادر و جنین”.

Results: Most studies mention high levels of mother’s pain, low Apgar score in the first minute, more changes in mother’s blood sugar, more bleeding, uterine atony, the possibility of unsuccessful intubation and the consequent risk of aspiration, and in some cases sore throat, muscle aches etc. as the complications of general anesthesia. In addition, some of these studies reported headache, nausea and vomiting, increased risk of infection, pruritus, chills, impotence, and in rare cases, meningitis and spinal cord injury as complications of spinal anesthesia.

Conclusion: In cesarean section, the complications of general anesthesia are much greater than spinal anesthesia. However, it should be considered that serious complications of spinal anesthesia are very rare compared to general anesthesia, but what is certain is that the complications of general anesthesia and spinal anesthesia should be explained by anesthesiologists to mothers who want to have a selective cesarean section and select the type of anesthesia by taking into account the cause of the cesarean section, the condition of the mother and baby, and the complications of each procedure.

Keywords: cesarean section, anesthesia, general anesthesia, spinal, fetus

Evaluation of the effect of antibacterial nano-particles containing Trachyspermum Copticum essential oil by Mozaffari method (Research Paper)

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Introduction: The aim of this study was to evaluation of the effect of antibacterial of nano-particles containing Trachyspermum Copticum's essential oil. For this purpose, the lipid system containing Trachyspermum Copticum's essential oil has been synthesized for gram-positive (Staphylococcus aureus) and gram-negative (E.coli and Pseudomonas aeruginosa) antibacterial methods as nosocomial infections.

Methods: The type of study is laboratory research. The nanoparticle synthesis method is Mozaffari method. Particle characterization has been performed in terms of size and charge with DLS and morphology with the Atomic Force Microscope (AFM) and the amount of loading and release with the spectrophotometer. MIC and MBC tests were then performed to evaluate the performance of nanoparticles containing Trachyspermum Copticum's essential oil on Staphylococcus aureus, E.coli and Pseudomonas aeruginosa.

Results: The average particle diameter was 70 nm and its zeta potential was -17.8 mV. The loading rate in nanoparticles was 54%, which was calculated by reading the absorption of light from the standard Trachyspermum Copticum curve. The minimum inhibitory concentration (MIC) of Staphylococcus aureus, E.coli and Pseudomonas aeruginosa for nanoparticles was 15.625, 31.25, 31.25 mg / ml. The minimum bactericidal concentration (MBC) of Staphylococcus aureus, E.coli and Pseudomonas aeruginosa for nanoparticles was 31.25, 31.25, 62.5 mg / ml.

Conclusion: Nanoparticles containing Trachyspermum Copticum's essential oil kill Staphylococcus aureus, E.coli and Pseudomonas aeruginosa as nosocomial infection and can be used as antibacterial nanoparticles.

Keywords: Trachyspermum Copticum, Nanoparticle, Antibacterial, Nosocomial infections

Evaluation of the effect of aqueous extract of Glycyrrhiza glabra and Echinophora cinerea on the tooth decay agent (Review)

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Introduction: Oral infections and tooth decay are still considered as one of the most important health problems, especially in developing countries. Glycyrrhiza glabra and Echinophora cinerea extracts contain medicinal herbal compounds that have the ability to suppress pathogens associated with tooth decay. The aim of this study was to investigate the antibacterial effect of the mentioned plants on Streptococcus mutans.

Methods: In this experimental study, the hot extraction method was utilized for Glycyrrhiza glabra and Echinophora cinerea root extractions. The extracts were analyzed by broth microdilution method to find the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of aqueous extracts on Streptococcus mutans to compare antibacterial effects.

Results: MIC of Glycyrrhiza glabra and Echinophora cinerea aqueous extracts for Streptococcus mutans was 1.95 and 3.91 mg/ml and their MBC was 3.91 and 7.81 mg/ml, respectively.

Conclusion: The findings of this study showed that the aqueous extract of Glycyrrhiza glabra root and Echinophora cinerea have significant antibacterial effects against Streptococcus mutans, but the aqueous extract of Glycyrrhiza glabra root has significantly stronger antibacterial effect compared to aqueous extract of Echinophora cinerea on Streptococcus bacteria.

Keywords: Tooth Decay, Streptococcus mutans, Glycyrrhiza glabra, Echinophora cinerea, Antibacterial effect

Evaluation of the effectiveness of physical activity on the general health of elderly women (Review)

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Introduction: It is one of the prominent phenomena in the field of health and old age. The goal of health programs for elderly women is to reduce the effects of chronic diseases, maintain the ability to live independently and improve their quality of life. The aim of this study was to evaluate the effectiveness of physical activity on the general health of elderly and postmenopausal women

Methods: The research is a review research and has been done by collecting materials from reputable articles on scientific sites such as sid, pubmed, etc.

Results: Findings show that active postmenopausal women have significantly better general health than inactive postmenopausal women. With an in-depth look at the situation of female elderly from various dimensions such as physical, mental, family, social, etc., we find that despite efforts and improvements in the health, social and economic status of Iranian women, there is a difference in indicators. Social and demographic health of elderly women compared to older Iranian men can be due to the unequal status of health and social health of women compared to men

Conclusion: In general, the results showed that exercise and physical activity promote the average general health and happiness of postmenopausal women. Due to the increase in the population of postmenopausal women, it is necessary to think of measures in order to improve the health of the society in order to do more sports activities for this group

Keywords: old age, general health, exercise and physical activity

Evaluation of the effects of a new drug derived from the combination of ninhydrin with Mafenide on Pseudomonas aeruginosa (Research Paper)

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Introduction: Pseudomonas aeruginosa is an opportunistic nosocomial pathogen. This organism is resistant to different groups of antibiotics. Infections caused by this organism due to antibiotic resistance may eventually lead to death. It is a gram-negative, aerobic, oxidase-positive and motile bacteria. Mafenide is a sulfonamide that has a bacteriostatic effect against many gram-negative and positive bacteria such as Pseudomonas aeruginosa and specified strains of anaerobes. It is absorbed through areas without blood vessels and is rapidly metabolized and excreted by the kidneys. Ninhydrin (Dihydroxy Indane-13-dione-22) is a chemical used to identify type I amines and type II amines. A chemical synthesis begins with the selection of compounds known as reactants. Various types of chemical reactions can be performed on these compounds to synthesize a particular product. In order to obtain new pharmaceutical compounds and increase antibacterial properties, new derivatives of Mafenide were synthesized.

Methods: 0.1 mmol of Mafenide acetate and 0.1 mmol of ninhydrin in 10 ml of ethanol was reflux for 3 hours. The reaction progress was controlled using thin-layer chromatography (TLC) in a normal hexane-ethyl acetate tank in a ratio of (1: 4). The solvent was evaporated, the precipitate was crystallized with 2-propanol solvent. Finally, the structure of the synthesized compound was confirmed by determining the melting point, C-NMR, H-NMR, TLC and IR. Then the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the synthesized drug on Pseudomonas aeruginosa were determined exerting well method on Müller-Hinton agar medium.

Results: Different colour and melting point and the results of C-NMR, H-NMR, TLC and IR indicate the new structure of the synthesized drug. The MIC and MBC of Mafenide on Pseudomonas aeruginosa were 0.5 and 1 mg/ml, and for the new derivative of Mafenide were 0.3 and 0.5 mg/ml.

Conclusion: According to the results, the synthesized drug has a more effective antibacterial activity against Pseudomonas aeruginosa than the base drug which

can be used as an ointment in burn patients and people with bedsores after secondary evaluation.

Keywords: Mafenide Acetate, Reflux method, Pseudomonas aeruginosa, Drug resistance, Antimicrobial effect

Evaluation of the inhibitory effect of Curcumin on Bcr-Abl Tyrosine Kinase Enzyme in Chronic Myeloid Leukemia by bioinformatics simulation method (Research Paper)

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Introduction: Chronic Myeloid Leukemia (CML) is a type of Leukemia that affects the cells that make up bone marrow tissue. This type of chronic leukemia is caused by a small, abnormal chromosome in the blood and bone marrow called the Philadelphia chromosome, or Ph1. The Philadelphia chromosome is caused by the reciprocal translocation of the long arm of chromosome 22 with the long arm of chromosome 9. This reciprocal translocation causes the transfer of ABL (Abelson) cellular oncogenes from chromosome 9 to chromosome 22 in an area called fracture aggregation, or BCR,which produces a chimeric transcript derived from the c_ABL (70%) and BCR genes. The expression of this chimer gene is a fusion protein with BCR protein at the amine terminus and ABL protein at the carboxy terminus, which is associated with transforming activity. The BCR-ABL protein produced stimulates the production of large amounts of the protein Tyrosin Kinase, which increases cell proliferation and inhibits apoptosis and does not depend on cellular signaling pathways and it causes uncontrolled proliferation of abnormal cells and it causes a deficiency of normal blood cells. Curcumin in turmeric is an effective substance that destroys brain plaques. Curcumin triggers programmed cell death pathways or apoptosis if it can enter cancer cells and it does this by activating caspases 3, 7 and 9. The aim of this study was to compare the effect of Curcumin on the enzyme Tyrosine Kinase Bcr-Abl and the drugs used to inhibit this enzyme by bioinformatics simulation method.

Methods: The structure of Tyrosin Kinase Bcr-ABL(with Accession = 5OC7) enzyme was received from NCBI website (www.ncbi.nlm.nih.gov/protein) in .PDB format and energy minimization experiment were performed on GROMACS 4.6.5 software. This structure then refined for blind docking experiments in HEX 8.0.0. Structures of Drugs of Bosutinib, Dasatinib , Erlotinib , Imatinib , Nilotinib, Omacetaxine, Ponatinib and Curcumin were obtained from pubchem website (www.pubchem.ncbi.nlm.nih.gov) in .sdf format and converted .pdb format by OpenBable2.3.2 software and optimized in HyperChem7 software. The Malecular docking experiments were done using drugs to study their interactions and to survey their bind sites. Docking results were analyzed by ArgusLab, Raswin, WebLab Viewer, Excell2016 and LigPlus software.

Results: The results of this study showed that Curcumin, Erlotinib, Nilotinib and Imatinib bind to both enzyme chains and show greater inhibitory ability; and Ponatinib and Bosutinib are more closely linked to the C chain, while Omacetaxine and Dasatinib are more closely linked to the A chain. The maximum hydrophobicity coefficient of the binding site is related to Ponatinib which tends to bind to hydrophobic amino acids and the minimum hydrophobicity coefficient belongs to Dasatinib which tends to bind to hydrophilic amino acids in the active site. The

results of this study showed that Nilotinib, Ponatinib and Imatinib have more negative binding energy.

Conclusion: Chronic Myeloid Leukemia is caused by a reciprocal translocation on chromosomes 9 and 22 and the formation of the Philadelphia chimeric chromosome and it follows the proliferation and incomplete evolution of white blood cells and is one of the most common cancers in children. This disease produces very large amounts of blood cells that are different from normal blood cells and stop the production of normal white blood cells, and reducing a person's ability to fight disease. These mutated cells also reduce the production of other blood cells, such as Red Blood Cells and Platelets, and are found in immunosuppression, anemia, and blood clotting disorders. In this study, it was observed that molecular weight and binding energy have a negative correlation with Sig = 0.020 and P-Value = -0.789 and by increasing the values of molecular weight , the binding energy is further reduced. Curcumin has a greater inhibitory effect than Erlotinib, Imatinib and Nilotinib due to its lower molecular weight.

Keywords: Curcumin, Tyrosin Kinase Bcr-ABL, Docking, Chronic Myeloid Leukemia, Philadelphia Chromosome

Evaluation of the relationship between PI3K oncogene expression changes in Jurkat E6.1 acute lymphoblastic leukemia cell line treated with NI chemotherapy (Research Paper)

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Introduction: Leukemia is characterized by the excessive growth of blood cells that affects the bone marrow. It can also be seen in adults, especially people over 65 years. The aim of this study was to evaluate changes in the expression of AKTPI3K signaling pathway PI3K gene in acute lymphoblastic leukemia cell line Jurkat E6.1 under treatment with NI.

Methods: NI was prepared at different concentrations (2,5 macro molar).The Jurkat E6.1 cancer cells were treated with chemotherapy after the cell passage in (48 hours). RNA extraction and Cdna synthesis were performed and the PI3K gene expression was evaluated by Real Time PCR. The results were analyzed by REST analaysis softwere.

Results: The results of this study showed that PI3K gene in concentrations (2 and 5 macro molar) in 48 hours showed a significant decrease ($p<0.001$) from the expression level of the gene.

Conclusion: : PI3K gene expression changes are influenced by the NI drug and decrease the expression of this oncogene in all concentrations and time, depending on time and concentration. The results of this study can be used to control and treat the optimal treatment of patients with leukemia, by identifying molecular pathways in the function of the chemotherapy drugs used, as well as introducing new drugs and preventing untreated control of JURKAT cancer cells.

Keywords: Acute lymphoblastic leukemia, PI3K, NI, Jurkat E6.1

Evaluation of trace elements and blood biochemical parameters in diabetic rats supplemented with Spirulina platensis microalgae: Investigation of mechanism by antioxidant enzymes in liver (Research Paper)

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Introduction: Objectives: Lipid peroxidation and hyperglycemic are known as common signs for diabetes. On the other hand, antioxidants, such as Spirulina platensis microalgae (SPM), may prevent lipid peroxidation and hyperglycemic. Thus, this study aimed to evaluation the antioxidant mechanism of SPM on lipid peroxidation and hyperglycemic in diabetes rats.

Methods: Methods: Sixty-four rats were grouped to 8 groups (n=8) and orally treated with 0, 10, 20, 30 mg.kg-1 body weight of SPM extract. Experimental groups were as follows; diabetic rats fed with 0 mg.kg-1SPM (DC), 10 mg.kg-1 SPM, 20 mg.kg-1SPM and 30 mg.kg-1 of SPM, respectively. Healthy rats were treated with 0 mg.kg-1 SPM (HC), 10 mg.kg-1 of SPM, 20 mg.kg-1 of SPM and 30 mg.kg-1 SPM. At the end of trial, blood samples were collected and the plasma concentrations of trace minerals (TMs), biochemical parameters, antioxidant enzymes in liver were assessed.

Results: Results: Our findings showed that diabetes significantly lowered the plasma concentration of TMs and antioxidant enzymes in liver and also increased the levels of malondialdehyde, glucose and lipid profile (DC vs. HC), but oral supplementing with SPM, (20 and 30 mg.kg-1 body weight), lowered levels of malondialdehyde level, glucose and lipid parameters. The same levels increased the plasma contents of zinc, iron, copper and selenium and activity of antioxidant enzymes ($P<0.05$).

Conclusion: Conclusion: It can be concluded that diabetes lowered TMs concentration and antioxidant enzymes and also increased lipid profile and glucose concentration, but SPM supplementing (20 and 30 mg.kg-1 body weight) increased some TMs and antioxidant enzymes. SPM may provide TMs for synthesis of antioxidant enzymes which subsequently enzymes reduce lipid profile and glucose concentration.

Keywords: Keywords: Antioxidant enzymes, Diabetes, Lipid profile, Plasma selenium, Spirulina platensis

Evaluation of urinary tract infection and drugs affecting it (Research Paper)

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Introduction: Urinary tract infection is one of the most common infections, mainly due to the presence and growth of microorganisms in the urinary tract. the antibiotic resistance pattern of this infection varies in different areas. the aim of the present study is to identify the bacterial etiology causing infection and susceptibility pattern as well as antibiotic resistance in patients referred to valiasr hospital in kazeroon and dr. soroori laboratory in darab.

Methods: UTI is a type of inflammatory response to the invasion of infectious agents, including bacteria. Different microorganisms can enter the bladder through the urethra and move toward the kidneys.If the bacteria in the lower parts of the urethra do not contaminate the bladder, the patient suffers from burning and pain during urination. If the bacteria contaminate the upper portions of the urethra, such as the kidneys, they are called inflammation of the kidney (pyelonephritis) And the patient experiences symptoms such as abdominal pain, nausea, vomiting, severe fever and chills. This infection is more common in all ages and individuals, especially in women and among women in pregnant women.

Results: Among 5414 samples in kazeroon, the results of urine culture of 2670 individuals were positive; 64 men and 2606 women. among 1192 samples in darab, the urine culture of 721 individuals was positive; 8 men and 721 women. the most common isolated bacteria were escherichia coli and epidermidis in darab and saprophyticus in kazeroon. based on antibiogram results in kazeroon most susceptibility was norfloxacin and most resistance were gentamicin.and kotrimoksazol , according to antibiogram results in darab, most susceptibility belonged to ciprofloxacin and cefixim and most resistance belonged to gentamicin and vancomycin.

Conclusion: Considering the obtained findings gentamicin , had the most resistance and norfloxacin and ciprofloxacin had the most susceptibility. therefore, gentamicin is not a suitable medicine for treatment.

Keywords: Vancomycin, Escherichia coli, Urinary culture, Antibiotic resistance, Disc diffusion.

Evaluation the effect of of topical use of the adipose stem cells (ASCs) with conditioned media (CM) in the treatment of atrophic acne scars with microneedling (Research Paper)

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Introduction: This study was to investigate the effect of topical use of the adipose stem cells (ASCs) with conditioned media (CM) in the treatment of atrophic acne scars.There is no gold standard treatment for facial acne scars, and overall, little literature exists about the combination therapy for treatment of acne scar. Microneedling is a very simple, safe, effective, and minimally invasive therapeutic technique. It was initially introduced for skin rejuvenation, however, now it is being used for a very wide range of indications including acne scar, acne, post-traumatic/burn scar, alopecia, skin rejuvenation, drug delivery, hyperhidrosis, stretch marks, and many more.

Methods: Fifteen patients with atrophic acne ulcers received four microneedling sessions 2 weeks apart on both sides of the face. The ADSC-CM was then placed locally on the right side of the face during microneedling. Clinical examination was performed by histopathological and computer histometric analysis before each session.

Results: The age of the patients varied from 24 to 40 years (mean: 30.08±4.94 years). Only nine patients (36%) were males. Clinical assessment by two-blinded dermatologists showed statistically significant improvement in the combination Microneedling+ ADSC-CM group. Patient satisfaction was statistically significantly better in the combination group (P=.001).There was significant increase in the improvement percentage of acne scars on right side microneedling + ADSC-CM(P=0.01) vs left side of face microneedling. Histologically, improvement of character of collagen and elastic fibers was noticed, especially on right side. Meanwhile, significant increase in epidermal thickness on both sides of face was detected.

Conclusion: conditioned media of adipose derived stem cells combined with microneedling is more effective in management of atrophic acne scars than microneedling alone. The combination of Microneedling and ADSC-CM is a safe and effective modality for atrophic acne scars. Additional randomized clinical study with long-term follow-up is necessary for further evaluation of ADSC-CM in combination with other procedures.

Keywords: Atrophic acne scars , Microneedling , Stem cell , Skin care , ADSC-CM

Evaluation the toxicity of Quercus infectoria extract on some biochemical and hematological parameter in mice (Research Paper)

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Introduction: Today, plants and their components have an important role in the treatment of diseases. Therefore, due to the increasing use of plant compounds, each plant product should be evaluated in terms of toxicological properties before being used in pharmaceutical form. This research was designed to assess the acute and subacute toxicity of Quercus infectoria extract on hematological and some serum biochemical parameters in mice.

Methods: Plant materials were collected from villages in Lorestan province, west of Iran. To determine the acute toxicity, four groups of mice (each group includes 6 mice) received different doses (0.5, 1, 2, and 4 mg/kg) of Q.infectoria extract orally. Sub-acute toxicity was performed by examining the biochemical and hematological parameters of forty treated mice after consuming different doses (150, 300 and 600 mg/kg) of Q.infectoria extract, orally for 14 days.

Results: The acute toxicity (LD50) tests of the oral administration of Q. infectoria extract, showed an estimated value of LD50 of mg/kg and the maximum nonfatal dose of mg/kg.

Conclusion: The findings demonstrated that orally administration of Q. infectoria at the doses of 150, 300 and 600 mg/kg for 14 days had no significant toxicity on the serum hematological and biochemical parameters.

Keywords: Quercus infectoria, Mice, Acute toxicity, Sub-acute toxicity

Evalution the efficacy of hydroalchoholic extraction of Verbascum Thapsus.L leaves in rat burn wound model (Research Paper)

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Introduction: Wound healing has always been a major concern for physicians and dermatologists, and burn healing is still a challenge in modern medicine. Burn wounds are one of the main causes of superficial scars on the body, which may lead to abnormalities such as isolation or depression regardless of the problem of treatment and cost. Verbascum thapsus.L is a plant of the scorphulariacea family. This plant has several therapeutic uses in traditional medicine, including the treatment of burn wounds. Also, according to previous studies, its antibacterial and healing effects have been proven. In this article, the efficacy of topical application of hydroalcoholic extract of Verbascum leaves in the second-degree burn wound model in male rats is evaluated.

Methods: After dentification and preparation of hydroalcoholic extract of Verbascum leaves by using percolation method, a topical formulation was made by inserting the extract into the eucerine base.Fallowing burn wounds induction, 30 male wistar rats were randomly divided into 5 groups: Sham positive control " silver sulfosodiazine ointment", negative control "Eucerine" as ointment base, and two groups 2.5% and 5% w/w of plant extract formulation . All groups received specific medication every 24 hours and dressing was changed every day.By photographing the wound surface over a period of 21 days, the percentage of wound healling and contraction were examined. On the last day of examination, all rats sacrificed and process of wound tissue healing and histological changes were evaluated.

Results: Macroscopic examination of the wound surface showed a significant size reduction in burn wounds of rats receiving 2.5% and 5% extract, which was more noticeable in the 5% extract group. In addition, based on histopathological evaluation, fewer inflammatory cells were observed in the wound tissue of rats treated with the extract formulations compared to 3 other groups. Also, epithelialization and increase in the number of new capillaries in the two groups receiving 2.5% and 5% extract were significantly higher than the other groups and the wound tissue in the extract group was almost completely healed.

Conclusion: Topical formulation containing hydroalcoholic extract of Verbascum leaves can be used as an herbal product to heal burn wounds.

Keywords: Verbascum thapsu , Mullen , rat , burn wound , wound healing

Exogenous sources of some nutrients and growth factors for peripheral nerve regeneration (Review)

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Introduction: Peripheral nerve injuries can be caused by accidental lacerations, congenital defects, surgical intervention, or other related conditions. Upon peripheral nerve damage, downregulation of neurotrophic factors results in reducing the chance of nerve regeneration. Therefore, using exogenous sources of some nutrients and growth factors including vitamins, glucocorticoids, gangliosides, and plant extracts can improve nerve damage recovery.

Methods: Some of the growth factors that have been widely used in the peripheral nerve regeneration include NGF, GDNF, CNTF, BDNF, neurotrophin 3, VEGF, insulin-like growth factor 1, leukemia inhibitory factor, glial growth factor, platelet-derived growth factor, and fibroblast growth factor 1. Many studies have shown that various types of vitamins such as vitamin B complex, vitamin B12, vitamin E, vitamin D3, vitamin D2, and vitamin C are effective in nerve regeneration. In addition, joint application of Radix Hedysari plant extract, an herbal preparation often used in traditional Chinese medicine, combined with a chitin conduit could efficiently promote the growth of lateral buds in the proximal nerve stump and considerably improve regeneration in a peripheral nerve injury model have also demonstrated that Salidroside, a derivative of Rhodiola rosea L. plant, can promote nerve regeneration in cellular nerve scaffolds through salidroside-induced neurotrophin secretion in SCs. Another key factor in tissue engineering is the addition of nanoparticles that can enhance nerve regeneration. Currently, nanoparticles have shown great potential in diverse therapeutic applications. For example, it has been shown that gold nanoparticles have beneficial effects on nerve regeneration. Some examples of effective nanoparticles in nerve repair include silver nanoparticles, magnetic nanoparticles, and iron oxide nanoparticles.

Results: Therefore, it seems that the administration of nutritional supplements has additional useful effects on nerve regeneration

Conclusion: In this review presents different types of exogenous factors used to repair peripheral nerve injuries. These include some nutrients and growth factors.

Keywords: Peripheral nerve, Regeneration, Growth factors, Nutrients

Exosomes: A promising strategy for Huntington's treatment (Review)

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Introduction: Exosomes are a subset of extracellular vesicles that are usually between 30 and 100 nanometers in size and can secrete a variety of cells. Exosomes can contain a variety of proteins, mRNAs, and miRNAs that regulate cellular communication and activity. Stem cell-derived exosomes have a potential for use in the treatment of incurable disorders, including HD. Huntington's disease (HD) is a progressive and autosomal dominant neurodegeneration caused by CAG expansion in the huntingtin gene (HTT), but the pathophysiological mechanism of mutant HTT (mHTT) remains unclear. Various studies have shown the effectiveness of exosomes in the treatment of Huntington's, so this study attempts to review this researches.

Methods: Huntington's disease (HD) is a progressive autosomal dominant neurodegenerative disorder caused by abnormal CAG repeats in the huntingtin gene, resulting in the production of mutant huntingtin (mHtt). The accumulation of mHtt aggregates causes striatal cell death through transcriptional dysregulation, activation of intrinsic apoptosis pathways, mitochondrial dysfunction, and altered protein-protein interactions. Dysregulated mitochondrial activation has been detected in the brains of both HD patients and transgenic HD mice, and mitochondrial dysfunction is a major causative factor in neurodegenerative disorders. Recent studies have shown that activation and protection of mitochondria using stem cells delays the progression of in vitro and in vivo HD. Downregulation of the p-CREB-PGC1α pathway is associated with mitochondrial dysfunction in HD; therefore, this pathway is a potential therapeutic target.

Results: Paracrine factors of stem cells, including exosomes, has therapeutic potential on many neurodegenerative diseases, including HD. Studies have shown that Exosomes from adipose-derived stem cells decreases the accumulation of mHtt aggregates, activates the p-CREB-PGC1α pathway, and modulates apoptotic expression proteins. In Huntington's disease, one of the most important miRNAs whose expression is reduced is miR 124, which plays a critical role in the expression of neurotrophic factors. In some research using exosome engineering, these miRNAs have been used by exosomes to treat Huntington's disease. Other miRNAs linked to HD, such as miR-22, a "perturbation" molecule due to its neuroprotective properties in an HD cell culture platform and miR-214, miR-150, miR-146a, and miR-125b that target the Htt gene are all found in exosomes.

Conclusion: In this study, the regenerative and neurotrophic effect of exosomes in Huntington's disease was investigated. Exosomes may be ideal carriers for the delivery of therapeutic agents to tissues that are difficult to access, such as those in the brain. Methods of isolating exosomes from blood, urine, or saliva in vivo and conditioned medium in vitro have been developed. However, the levels of exosome cargos, such as proteins or non-coding RNAs, are too low for accurate quantification or analysis, given the ineffectiveness of the drugs used in Huntington's disease, which only slow the progression of the disease, the use of exosomes could be a promising future treatment for the disease. Methods of isolating exosomes from blood, urine, or saliva in vivo and conditioned medium in vitro have been developed. However, methods for obtaining large volumes of exosomes for future treatment should be considered.

Keywords: Exosomes, Huntington's disease, miRNA

Expression and Clinicopathological Significances of lncRNAs: Could ARA and ZEB2NAT be the Potential Breast Cancer-Related Biomarkers? (Research Paper)

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Introduction: Pieces of evidence have shown that a significant proportion of cancer-prone factors are not attributed to alterations in protein-coding sequences. Adriamycin resistance-related (ARA) and natural antisense of ZEB2 (ZEB2NAT) long non-coding RNAs (lncRNAs) have been indicated with oncogenic properties by regulating various signaling pathways and epithelial-to-mesenchymal transition (EMT), which may have diagnostic and prognostic potential as a novel group of biomarkers. The current study aimed to evaluate the expression status of ARA and ZEB2NAT lncRNAs and their clinicopathological significance in a population with breast cancer (BC).

Methods: Total RNA was extracted from 60 tumor samples and their normal adjacent tissues (NATs). The lncRNA expressions were measured using quantitative reverse transcription PCR (RT-qPCR) and statistical analyses were performed by SPSS version 25.

Results: Our data showed a significant upregulation of ARA and ZEB2NAT lncRNAs in tumor tissues compared to NATs ($p < 0.001$; $p = 0.021$, respectively). ARA and ZEB2NAT expression were observed to be significantly associated with tumor grade, nuclear grade, tumor stages, and lymph node metastasis ($p < 0.05$). Additionally, ARA expression was significantly correlated with breastfeeding status ($p = 0.027$).

Conclusion: Our data revealed that ARA and ZEB2NAT lncRNAs were overexpressed in BC. Furthermore, the selected lncRNAs were found to might be the potential biomarkers for BC diagnosis and prognosis. However, the findings of the current research are required to be replicated in other studies with larger sample sizes.

Keywords: Breast cancer, long non-coding RNA, Biomarker, ARA, ZEB2NAT

Fabricating Nerve Conduits with Proper Candidate Materials Can Increase Chance of Peripheral Nerve Regeneration (Review)

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Introduction: Introduction Peripheral nerve damage is a common clinical complication of traumatic injury occurring after accident, tumorous outgrowth, or surgical side effects. Although the new methods and biomaterials have been improved recently, regeneration of peripheral nerve gaps is still a challenge. In a small nerve injury with gap less than 1cm, regeneration is possible when two nerve stumps can be brought together (i.e. end-to-end suturing) without tension. In the larger peripheral nerve gaps, it is possible to regenerate PNS injury by applying the procedure of rejoining of nerve segments including implantation of autografts, the gold standard method, andinsertion of artificial nerve guidance conduits (NGCs) between nerve stumps. However, autologous nerve graft approaches are limited by donor site morbidity, increased surgical complications, diameter mismatch between the recipient nerve and the graft. In this situation, the application of biodegradable nerve conduits made by tissue engineering would involve protecting the nerve from interference the surrounding tissue, directing the regenerating axons from the proximal stump into the distal nerve stump and playing a more significant clinical role to regenerate the nerve better. The conduit is tubular structure designed to bridge nerve injury sites; it acts as a guide for the regenerating nerve stumps. To facilitate neural regeneration, an ideal nerve guidance conduit (NGC) should possess particular properties including biodegradability, biocompatibility, permeability, flexibility, low-toxicity, having anti-microbial activity, well-aligned orientation, proper porosity and minimal swelling, being conductive, nutrient diffusible and controlled release of drugs and neurotrophic factors capability. Different biomaterials used for fabricating nerve guidance conduits are classified into natural and artificial materials. Due to their ability to mimic the extracellular matrix (ECM), some natural biomaterials such as laminin, collagen, elastin, hyaluronic acid and fibrinogen have been of great interest to investigators, particularly in the field of nerve tissue engineering. Chitosan, alginate and silk fibroin (SF), are also three natural polymers widely used in tissue engineering. One of the major challenges in using natural polymers in tissue engineering is their poor mechanical properties. Synthetic polymers are another type of materials that have been frequently used for the fabrication of nerve conduit. Compared with their natural counterparts, synthetic polymers have advantages such as tunable mechanical properties and tailorable properties via modulating their chemical properties. However, they have shown some limitations in terms of transplant rejection. Some of synthetic polymers include poly (L-lactic acid) (PLLA), poly (ε-caprolactone) (PCL), Poly (lactic-co-glycolic) acid (PLGA) Silicone polymer and Poly (dimethylsiloxane) (PDMS). However, much research is currently underway to develop artificial nerve conduits which may serve as guiding channels for regenerating axons thus reducing the need for donor tissue. In this Review

presents different types of artificial nerve grafts used to repair peripheral nerve injuries. These include synthetic and natural polymers. Also, the effect of their repair on peripheral nerve damage in recent research has been investigated.

Methods: Different biomaterials used for fabricating nerve guidance conduits are classified into natural and artificial materials. Due to their ability to mimic the extracellular matrix (ECM), some natural biomaterials such as laminin, collagen, elastin, hyaluronic acid and fibrinogen have been of great interest to investigators, particularly in the field of nerve tissue engineering. Chitosan, alginate and silk fibroin (SF), are also three natural polymers widely used in tissue engineering. One of the major challenges in using natural polymers in tissue engineering is their poor mechanical properties. Synthetic polymers are another type of materials that have been frequently used for the fabrication of nerve conduit. Compared with their natural counterparts, synthetic polymers have advantages such as tunable mechanical properties and tailorable properties via modulating their chemical properties. However, they have shown some limitations in terms of transplant rejection. Some of synthetic polymers include poly (L-lactic acid) (PLLA), poly (ε-caprolactone) (PCL), Poly (lactic-co-glycolic) acid (PLGA) Silicone polymer and Poly (dimethylsiloxane) (PDMS).

Results: However, much research is currently underway to develop artificial nerve conduits which may serve as guiding channels for regenerating axons thus reducing the need for donor tissue.

Conclusion: In this Review presents different types of artificial nerve grafts used to repair peripheral nerve injuries. These include synthetic and natural polymers. Also, the effect of their repair on peripheral nerve damage in recent research has been investigated.

Keywords: Biomaterial, Nerve conduits, Peripheral nerve, Regeneration, Implantation

Fabrication and evaluation of nanoclay-enriched calcium phosphate granules for bone regeneration (Research Paper)

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Introduction: Tissue engineering is an essential field that provides alternative solutions for organ transplants, and contributes dramatic potential improvement in human health. Several types of bone graft materials have been used to restore damaged bones, including different types of porous materials, such as ceramics, polymers and metals have been developed in the field of tissue engineering. For the last few decades, calcium phosphate ceramics have attracted the attention of biomaterial scientists due to their osteoconductivity, biodegradability and biocompatibilities. One of the most important challenges facing tissue engineering researches is the scaffold design with optimum physical and mechanical properties for growth and proliferation of cells and tissue formation. CaPs materials such as β-tricalcium phosphate (Ca3(PO4)2, β-TCP) and hydroxyapatite (Ca10(PO4)6(OH)2, HA) are similar to those found in human bone; therefore, they are the most commonly used ceramics in the biomedical fields. Among these bioceramics, β-TCP has been widely used instead of apatites for oral plastic surgery and bone tissue engineering due to their excellent biodegradability so it can be resorbed and replaced by new formed bone tissues and there is no need for a second surgical operation to remove the device after healing occurrence. However, both of these ceramics have a number of drawbacks that have reduced their clinical performance. The biodegradation of HA was shown to be very low, which prevented optimal bone formation. On the other hand, β-TCP was reported to be a mechanically weak ceramic, so its biomedical applications for bone tissue reconstruction have been largely limited by their poor mechanical properties The aim of this study was to produce a novel nanocomposite containing β-tricalcium phosphate and nanoclay and then analyzing the capacity of osteogenic activity. To our knowledge, nanoclays have not been incorporate previously with β-tricalcium phosphate for fabrication of granules for bone grafting. Also this study is the first report on the effects of nanoclay on the mechanical properties and porosity of granules.

Methods: In this paper, nanocomposite powders were synthesized by precipitation processes. Then, the porous ceramic granules were prepared by the polyurethane sponge replication method. In this study four kinds of β-TCP granules with different nanoclay contents (ranging from 0.1 wt.% to 10 wt.%) have been prepared. X-Ray Diffraction (XRD) and Scanning Electron Microscope/Energy Dispersive X-ray spectroscopy (SEM/EDX) techniques were used in order to study the phase and element structure, morphology, and determination of functional groups of granules. Afterwards, the morphology, mechanical behavior, porosity of granules were

evaluated and the effects of nanocomposites on attachment, viability and proliferation of human mesenchymal stem cells were also investigated.

Results: Physiochemical characterizations demonstrated that the chemical composition and microstructure of the granules were similar to the natural spongy bone. Interconnected macro pores ranging over 200 to 500µm were observed for all kinds of granules. SEM micrograph images showed that human mesenchymal stem cells attached to the surfaces of the granules and were well proliferated. The results warranted that, the synthesized granules exhibit good biocompatibility and in vitro biomineralization. Porosity is an essential factor for bone tissue engineering. The results of porosimetry analysis indicated that adding nanoclay to β-TCP granules resulted in no significant change on the porosity percentage and according to SEM images, macropores and their interconnectivity was also maintained. The mechanical test proved that increasing the weight percentage of nanoclay to β-TCP granules caused an increase in compressive modulus. So, by increasing the nanoclay concentrations up to 10%, compressive strength was enhanced and the porosity has not been affected significantly

Conclusion: Based on the results of compressive strength and porosity tests, the most suitable type of granule is β-TCP + 10% nanoclay with 75±5% porosity, with a compressive modulus of 230 MPa, which can be utilized in bone tissue engineering. It is considerable that high porosity β-TCP granules with high initial strength have the advantage of immediate postoperative weight bearing. Therefore, this granule have great potential for bone defects regeneration and tissue engineering applications.

Keywords: Tissue engineering - β-tricalcium phosphate - nanoclay- granule-bone grafts

fabrication of PCL/Gelatin biocomposite with 3D printing and comparison of mechanical properties with electrospinning's sample (Research Paper)

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Introduction: both the natural polymers (including collagen and gelatin) and synthetic polymers (such as PLGA and PCL) have been commonly used as the condidates for electrospinning and 3D printing. Today;these two way of fabrication scaffolds are very common .obviously ;they have some differences.this research study how they differ in mechanical properties.

Methods: In the last research, the primitive scaffolds were prepared by FDM 3D printers , for using 3d printers we need to find suitable mode that these are as: Floor temperature: 35 ° C, Nozzle temperature: 160 ° C, Print speed: 1250 mm / min with automatic adjusting fan .after this step; gelatin have been mixed with twice distilled water at a ratio of 0.01 and stirred for 24 hours then polycaprolacton scaffold was sank in the mixture for a while and for crosslinking glutaraldehyde vapor used. In the light of http://dx.doi.org/10.1080/09205063.2016.1160560 they investigated 5 different ratio of pcl/gelatin properties that the best result in mechanical properties were for 4:1 and 2:1 pcl/gelatin.

Results: For Investigation of attachment of gelatin on polycaprolactone in 3d printing's scaffolds using scal(figure1) and the figure2 the mechanical properties of two samples in pure and composite form show that mechanical property of scaffold in composite form is more than pure one. In the other case (electrospinning samples figure3) the best result of mechanical properties are for 4:1 and 2:1 pcl/gelatin, additionally 2:1 sample is more better than 4:1.

Conclusion: However these two way of fabrication biocomposites are very common and both of them showed acceptable results, depends on where we use the scaffold it could be different .

Keywords: pcl/gelatin biocomposite - 3D printing - electrospinning - mechanical properties

Fabrication of polymeric micro-carriers to use in cell therapy in heart.

(Research Paper)

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Introduction: The rate of death among the people suffering from myocardial infarctions is six times more than other persons at the same ages. Because of the inability of conventional methods to regenerate the infarcted part of the heart, cell-based regenerative medicine emerges as a reliable approach. The goal of cell therapy is to form new and functional myocardial tissue by supplying various sources of stem cells. However, due to the low rate of residence and cell viability of the transferred stem cells and their low ability to transplant host tissue into the damaged myocardium, cell therapy has not been clinically efficient and need to develop it. Cellular carriers can be a suitable solution to enhance the survival of transported cells to the myocardium site. Among various methods to generate cell carriers, microfluidic devices are promising systems to fabricate micro-carriers with the minimum adverse effects on cells during the generation of micro-carriers and low invasiveness for their transplantation. The significant point to be mentioned is that those micro-carriers should preserve cells for a long time in order to be effective to regenerate the infarcted tissue.

Methods: A microfluidic device was used to generate micro-carriers with a co-flow microfluidic-based device. Alginate conjugated with phenol moieties (Alg-Ph) was synthesized and utilized as the main polymer because of its biocompatibility. The Alg-Ph was synthesized by combining alginate and tyramine hydrochloride in the existence of N-hydroxysulfosuccinimide(NHS) and N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide in amino reduction reaction. This modified polymer was polymerized by horseradish peroxidase (HRP) and hydrogen peroxide as an electron donor in designed coaxial microfluidic devices, whereas Alg-Ph, HRP, and A549 cell extruded from the inner channel and liquid paraffin saturated with H2O2 from the outer channel.

Results: The degree of Ph conjugation obtained at 1.7×10 -4 mole Ph/g Alg-Ph. We could fabricate spherical micro-carriers containing A549 cells, as a model cell, with radiuses of 70 ± 10 μm and high stability resulting from enzymatic reactions. Following micro-carriers in vitro indicated that they did not degrade after even 30 days, which not only proved their high stability but also made them suitable for delivering cells into the heart tissue. Moreover, trypan blue analysis confirmed that cells were alive within micro-carrier after 30 days, which meant that they could receive adequate oxygen and nutrition to be live.

Conclusion: Fabricated spherical micro-carriers can be a promising approach to solve the low survival of transported cells. As a result, this method can be proposed to improve the efficiency of cell therapy to regenerate infarcted heart tissue.

Keywords: Myocardial infarction, micro-carriers, microfluidic systems, Horseradish Peroxidase crosslinking

Factor V Leiden 1691G > A mutation and the risk of recurrent pregnancy loss (RPL): systematic review and meta-analysis (Review)

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Introduction: Although numerous replication case-control studies have attempted to determine the association between Factor V Leiden (FVL) 1691G > A mutation and susceptibility to Recurrent pregnancy loss (RPL), there have been confliction among the results of various ethnic groups. To address this limitation, here we implemented first meta-analysis to provide with consistent conclusion of the association between FVL 1691G > A mutation and RPL risk.

Methods: After a systematic literature search, pooled odds ratio (OR) and their corresponding 95% confidence interval (CI) were used to evaluate the strength of the association. Additionally, meta-regression analyses were performed to find potential source of heterogeneity.

Results: In this meta-analysis, 62 studies, containing 10,410 cases and 9406 controls, were included in quantitative analysis. Overall population analysis revealed a significant positive association in the dominant (OR = 2.15, 95% CI = 1.84–2.50, P < 0.001), over-dominant (OR = 1.88, 95% CI = 1.61–2.19, P < 0.001), allelic (OR = 2.05, 95% CI = 1.79–2.35, P < 0.001), and heterozygote (OR = 1.97, 95% CI = 1.68–2.30, P < 0.001) models. Moreover, a significant association of dominant (OR = 3.04, 95% CI = 2.04–4.54, P < 0.001), over-dominant (OR = 2.65, 95% CI = 1.74–4.05, P < 0.001), and heterozygote (OR = 2.67, 95% CI = 1.81–4.22, P < 0.001) models was found in the Iranian population. The subgroup analysis indicated strong significant association in Asian, European, Africa population, and case-control studies but not in South Americans and cohort studies.

Conclusion: The FVL 1691G > A mutation and the risk of RPL confers a genetic contributing factor in increasing the risk of RPL, particularly in Iranians, except for South Americans.

Keywords: Recurrent pregnancy loss, Factor V Leiden, 1691G > A mutation, Meta-analysis, Meta-regression

Factors affecting egg sensitivity in infants. (Review)

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Introduction: Eggs are usually oval in shape that are biologically laid for reproduction and are a food source for humans. infant is A child between 1 and 23 months of age. Allergy is an extreme reaction of the immune system to various factors. Eggs are the main cause of food allergies in young children, which is 2.4-2.6%. This sensitivity tends to manifest in the first 2 years of life. At least 24 different proteins in egg whites pass into the human body, known as allergens, and only some of them are allergenic and can cause an allergic reaction through IgE.

Methods: The reviewed articles are from1980-2019 . They are from scholar and pubmed databases. 15 articles were selected from scholar database, 7 articles were deleted due to non-compliance with the desired title, and 30 articles were selected from pubmed database, of which 12 articles were deleted. In the end, 26 articles were used to produce abstract.

Results: If proteins or egg yolk and egg white allergens are recognized by the immune system as a foreign agent and the response to rejection is sensitive. These proteins are usually in contact with the host's immune system through the gastrointestinal tract. Occasionally, contact of proteins or egg allergens can occur during fetal development through the placenta because studies have shown that IgE antibodies from the fetus to dietary proteins in the umbilical cord blood indicate that they are caused by Food antigens have been removed from the placenta. It is also recognizable that autoanti-idiotype antibodies cross the placenta, and some of them may provide an internal picture of the antigen and cause allergies. Egg proteins can cause allergies in infants during the early stages of a baby's life through breast milk, as new studies show that egg proteins have the power to pass into breast milk. They can also cause allergies through inhalation or skin contact. Another factor that causes sensitivity to egg ratio is a change in diet, for example, when new foods are introduced or when the mother is breastfeeding, complex physiological changes occur. This condition can have a profound effect on the immune response. Changes in the body's supervisory mechanisms alter the induction of tolerance, resulting in food allergies. Egg whites are more likely to cause an allergic reaction. The main allergens in egg white are ovomucoid and ovalbumi. ovalbumi maintains its immune system after 20 minutes of ovomucoid. Due to its resistance to heat and enzymatic digestion and its physical properties, egg whites are the most important protein that can cause allergic reactions. Canalbumin (Gal d3) and lysozyme (Gal d4) are more thermolabile and have weaker antigens, but can still cause allergic reactions if consumed more or less raw. Allergies to specific lysosomal IgEs may be responsible for allergic reactions to drugs or foods produced with this protein.

Conclusion: ccording to the reviewed articles, the result is that due to the fact that eggs are the main cause of allergies in infants and children, and even before the birth of the baby, there are effective factors in causing this allergy. The diet of pregnant and lactating mothers, infants and children should be monitored by a specialist.

Keywords: egg – infants– Allergens

Factors affecting on developmental delay in preterm infants (Review)

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Introduction: Preterm is defined as babies Born alive before 37 weeks of pregnancy are completed. Across 184 countries, the rate of preterm birth Ranges from 5% to 18% babies born.Every year an estimed 15 million babies are born preterm and this number is raising.Preterm birth complications are leading cause of death among children under 5 years of age responsible for approximately 1 million berth in 2015.In this regard we review recent studies on the causes of this problem and the factors that affect the development of these babies.

Methods: Search was done by keywords in Pubmed, Google scholar,Cochrane,irranmedix and SID, in the period of 1990-2020 . 200 articles were received. By studying the title of the articles, 20 articles were selected, then by studying the abstract of the articles, 12 articles were selected. All of Persian articles were deleted. Finally 8 articles used in this study.

Results: 4 experimental articles and 4 reviw articles that examined this subject,were analyzed.Among them,5 articles referred to the effect of nutrition,2 cases referred to the effect of postpartum measures and 1case referred to genetic factors.Iron-deficiency anaemia in 6-mo-old infants is associated with adverse effects on at least one aspect of CNS development.A small head circumference and white matter injury in the form of leukomalacia have been observed in population of infants with sever from of congenital heart defect.This delay in brain development may foster susceptibility to periventricular leukomalacia in the preoperative, intraoperative, and postoperative periods. Delaying enterel feeding could diminish the functional adaptation of the gastrointestinal tract and prolong the need for parental nutrition with its attendant infectious and metabolic risks. It is recommended that women increase their calcium intake during pregnancy and lactation of the dosage varies among personals.

Conclusion: According to studies,the mother’s nutrition during pregnancy and then childbirth,wich breastfeeding, should be considered and take supplements with breast milk.Also,measures such as the time of clamping the umbilical cord,the duration of the intubation,the long_term mechanical ventilation and the appearance of respiratory apena,etc that affect on the evolutionary process , must be considered.Complete monitoring of the mother's physical and mental condition during pregnancy and childbirth processes should be performed under the supervision of a specialist.

Keywords: preterm infants,delayed development,affective factors

Factors affecting urinary tract infection during pregnancy and its negative effects (Review)

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Introduction: Urinary tract infections are inflammatory responses of the urinary density epithelium to microbial attack. A pregnant woman is a condition in which a woman has an embryo or fetus in her womb. The human embryo is a diploid multicellular eukaryote that results from human reproduction.. The second most common complication in pregnant women and the most important infectious disease in Iran in 2013 is urinary tract infection, which is one of the main causes of cesarean section and is mainly due to the presence and growth of microorganisms in the urinary tract.

Methods: We searched PubMed, Google Scholar search engine with acute key words" urinary tract infections" , "pregnant women" and "human fetus". All articles were published between 1982 until 2020 and have ethical considerations. As a result of our research if our research, 42 articles were found respectively. All the studies, use human samples. After investigating their titles 15 articles were excluded and by reading abstracts 5 articles excluded. Finally, 22 articles were included.

Results: According to 9 articles, there is a risk of urinary tract infection from the beginning of week 6 to 24 of pregnancy. According to 3 articles, changing the temperature of the seasons is one of the main causes of urinary tract infections and the highest rate of urinary tract infections in pregnancy in winter. In the 9 articles mentioned, the most common bacterium that causes urinary tract infections during pregnancy is Escherichia coli. According to 9 articles, the increased risk of urinary tract infections during pregnancy is mainly due to the history of urinary tract infections as well as economic and social status, personal hygiene, personal characteristics, sickle cell disease and anemia, age, number of births, lack of care during pregnancy , Physiological changes during pregnancy in the urinary tract and endocrine system increase the risk of urinary tract infections. According to 8 articles, this complication increases the risk of mental retardation or delay in intrauterine growth as well as fetal death in the third trimester of pregnancy and reduces fetal weight and cesarean section. Other risks include anemia, high blood pressure, such as preeclampsia, the risk of miscarriage, and cystitis. According to another article, group B streptococcal infection causes abnormal urinary tract infections in infants, amnionitis, and preterm labor.

Conclusion: Until now the number of studies was done in this field was low. We can get more reliable results, if more studies tend to this field. According to the articles studied, the result is that uncontrolled urinary tract infections are a risk to maternal and fetal health. Therefore, preventive care should be done at all ages,

especially during pregnancy, and pregnant women should be tested for bacterial infections and should be treated by specialists if they notice the disease.

Keywords: Urinary tract infections, Pregnant women, Human fetus

Factors associated with sexual risk behaviors in women drug users: A review study (Review)

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Introduction: Substance use is known as an important underlying factor in the occurrence of risky sexual behaviors, while risky sexual behaviors can lead to STIs and HIV / AIDS, especially in women. Understanding the specific factors associated with sexual risk behaviors in women drug users can help identify high-risk individuals as the target group of interventions, and information on how to change the risk in this group of people Provide. Therefore, the present review study was conducted to identify the factors associated with sexual risk behaviors in women using drugs.

Methods: In the present review study to find research-related studies, in the period 2000 to 2019 from the Persian databases SID and magiran as well as English databases including Pubmed, Scopus, Elsevier, Weily online library, Web Of Sciences and Google Scholar search engine. Keywords including Sexual behavior, Unsafe sex, Drug users, Substance-related disorders, Women, Sexual risks, High-risk sexual behavior, HIV sexual behaviors substance use, risky sex, were searched. Out of 680 articles, 21 articles were eligible for research and were selected for this study

Results: The results of various studies addressing major issues in this group of women, including (1) the role of socio-demographic factors, (2) substance use, (3) engaging in sexual work (being a sex worker), (4) characteristics related to sexual partner, (5) gender roles, (6) love and trust, and (7) psychiatric problems. Although many of these factors seem to be interrelated and impossible to separate, the impact of some of these factors is more prominent and should be given more attention.

Conclusion: Given that it can be predicted that women will make up a large number of drug users in the future, and the accompaniment and formation of risky sexual behaviors in women users is significant and undeniable, so taking into account the factors And the factors obtained from the above study and the identification of high-risk individuals, as well as the necessary interventions in this field, can be hoped to some extent to prevent the formation of such behaviors in women drug users.

Keywords: sexual behavior, Unsafe Sex, Drug Users, Substance-Related Disorders, women

Fast identification of dermatophytes by MALDI-TOF/MS (Review)

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Introduction: Classical identification of dermatophytes relies on culture characteristics, microscopic morphology, physiological tests and clinical data. Their overlapping phenotypic characteristics, however, may be confusing and the identification requires growth of the organisms in culture for at least one week, which delays the diagnosis. Molecular techniques allow a fast and reliable identification of dermatophytes. ITS (Internal Transcribed Spacer) DNA sequencing is presently considered the gold standard for molecular identification and phylogenetic analyses of dermatophytes. However, DNA sequencing is expensive and at least 2–3 days are required before a sequence is obtained from a culture. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is now used routinely in clinical diagnostic laboratories as it is faster than PCR and requires little sample handling. It is a cost-effective and reliable technique for the identification and typing of microbial pathogens including bacteria, yeasts, and filamentous fungi. MALDI-TOF MS has already been used for the identification of dermatophytes, either after their isolation and cultivation or directly from clinical material.

Methods: The approach is based on the acquisition of a protein profile (between 2 and 20 kDa) and its comparison to a database with reference spectra. This MALDI-TOF MS-based identification technique analyzes the protein content from treated or intact cells of microorganisms under the form of a spectrum that is considered as a protein fingerprint specific of a micro-organism. An unknown microorganism is identified by comparing its spectrum with the spectra in the reference library. Four different MALDI-TOF MS benchtop platforms are now commercialized for the routine identification of fungi in clinical microbiology laboratories. Together with the Andromas (Andromas SAS, Paris, France) and the Axima@Saramis (Shimadzu/AnagnosTec, Duisburg, Germany) systems, the Bruker Biotyper (Bruker Daltonics, Bremen, Germany) and the Vitek MS (bioMerieux, Marcy l'Etoile, France) systems are currently employed in Europe, whereas only the latter two systems are approved by the U.S. Food and Drug Administration for clinical diagnostic use (albeit limited to bacteria and yeasts). In particular, the Bruker Daltonics instrument provides its own solution (i.e., MALDI Biotyper), which is comprised of software and a database, whereas the Vitek MS system integrates the SARAMIS (Spectral Archiving and Microbial Identification System) database (i.e., an open database made by AnagnosTec) with its own closed database. Biotyper software generates (log) score values ranging from 0 to 3, with scores of ≥2 and ≥1.7 being recommended for species-level or genus-level identifications, respectively, whereas a score (confidence) value of ≥60% is recommended for species-level identification using Vitek MS software. Despite differences with regard to sample preparation, spectrum preprocessing, and in silico identification algorithms, all these systems appear to be reliable tools for mold identification.

Results: Over the last 5 years, accumulated experience clearly shows that MALDI-TOF MS holds promise as an accurate mold identification tool, particularly with common filamentous fungal pathogens. Conventional phenotypic methods to identify filamentous fungi are relatively inexpensive but have a turnaround time of several days because of the time taken for fungal growth, which in certain groups of fungi (e.g., dermatophytes) can be very long. As a result, initial antifungal therapy of infection is empirical, and appropriate therapy may be delayed if antifungal resistance is not suspected. The turnaround time has been reduced by the introduction of MALDI-TOF MS instruments in the clinical laboratory routine, although these instruments continue to rely on fungal cultures. In this context, the MALDI-TOF MS technology is also being exploited to analyze patient specimens directly, completely bypassing the need for fungal growth.

Conclusion: The construction of expanded MALDI-TOF MS databases is labor-consuming, requires mycological skills, and is hindered by the fact that the IVD (in vitro device) versions of the commercialized MALDI-TOF MS systems do not enable the implementation of databases. Otherwise, in environments not subject to regulatory-body (i.e., FDA) restrictions, the practice of the expansion/improvement of a RUO (research-use-only) database (i.e., Biotyper or SARAMIS) should be confined to reference laboratories. Thus, while this practice will be a huge benefit for laboratories with large collections of clinical isolates, it should be mandatory that an identification strategy is expanded and validated with new isolates/ species and analyzed with other databases. In this context, efforts are needed to develop online-available reference spectrum databases that could be interrogated similarly to sequence databases such as the NCBI GenBank database.

Keywords: Identification, Dermatophytes, MALDI-TOF MS

feedback and performance of nursing students in the evaluation of Objective structured clinical examination based on the nursing process (Research Paper)

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Introduction: Today, it is important to conduct a valid test to evaluate the practical skills of nursing and the application of the nursing process in clinical evaluations. The aim of this study was to investigate the feedback and performance of nursing students using in the evaluation of Objective structured clinical examination (OSCE) based on the nursing process in 2019.

Methods: In this study which conducted in 2019, the number of 35 nursing students selected by consensus. The design of the osce stations was based on nursing processes. Data collection tools were a student feedback questionnaire to the osce test and a performance checklist. Data were analyzed using SPSS software and descriptive statistics, T-test and Pearson correlation.

Results: 68.6% of students received the overall score of the OSCE test at a good level. The lowest mean score (7.39 ± 3.41) was related to the nursing diagnosis station and the highest mean (19.21 ± 0.97) was related to the vital signs station. The minimum overall score of the test was 10.70 and the maximum total score was 17.75.

Conclusion: The findings of this study show the positive feedback of most students on this test and the importance of nursing processes in increasing the quality of nursing care. Therefore, it is recommended to use this method in evaluating the clinical skills of nursing students.

Keywords: Objective Structured Clinical Examination, Performance, Clinical Competencies, nursing processes

Gene Ontology and Biological Networks Analysis in Primary Normal Human Epidermal Keratinocytes (NHEK) Treated by Resveratrol (Research Paper)

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Introduction: Resveratrol is a plant polyphenol found in high concentrations in red grapes that has been proposed as a treatment for hyperlipidemia and to prevent fatty liver, diabetes, atherosclerosis, inflammation and aging. Resveratrol use has not been associated with serum enzyme elevations or with clinically apparent liver injury [1]. The fact that resveratrol is found in the skin of red grapes and as a constituent of red wine may explain the "French paradox". This paradox is based on the observation that the incidence of coronary heart disease is relatively low in southern France despite high dietary intake of saturated fats [2]. Resveratrol is a natural product that has gained tremendous interest due to multiple reported health-beneficial effects. However, the underlying mechanisms of its actions remained largely controversial. Major biological effects of resveratrol might be attributed to its bicarbonate-induced production of phenolic radicals and reactive oxygen species (ROS) such as superoxide and hydrogen peroxide under physiologically relevant conditions. Resveratrol treatment led to mild, Nrf2-specific gene expression reprogramming [3]. Here, we have analyzed transcriptome data produced by Annabell Plauth and colleagues, and by using system biology approaches, we examined gene ontology and networks analysis effect of resveratrol in primary normal human epidermal keratinocytes (NHEK).

Methods: We have used a microarray data (GEO accession number: GSE72119) that includes samples of Resveratol (RSV) versus control samples. First all, the data quality control was checked using boxplot, heatmap and principal component (PC) analysis. To obtain DEGs (Differentially Expressed Genes) between control and RSV, the Limma package was used, which is embedded in the R programming language. We have discarded all DEGs with adjusted P-value >0.05 and log 2 FC between ±1. We have used the Enrichr database to annotate DEGs. To build the gene network interaction, we entered the DEGs into the GeneMANIA server and the Protein-Protein Interaction network (PPI) was created with the STRING server. Finally, the transcription factors (TFs) and protein kinases (PTKs) were re-examined using the X2K web server.

Results: According to the boxplot, samples haves a median center, also PC analysis and heatmap confirmed that the dataset had a high quality. Microarray samples of RSV and controls were compared to identify DEGs. We detected the 1514 number of DEGs in the comparison between RSV and control. The DEGs were submitted to Enrichr database to identify genes related to annotations including Cellular Component, biological process, and molecular function. Gene network interaction and protein-protein interaction network were calculated and

constructed. Important transcription factors include: MYC, E2F1, SIN3A, E2F4, MAX, FOXM1, NFYA, NFYB and E2F6. Important protein kinases include: MAPK14, CDC2, CK2ALPHA and CDK4.

Conclusion: The gene expression profile of normal human epidermal keratinocytes was strongly changed by the treatment with 50μM concentration of Resveratrol. We predicted potentially important transcription factors and Protein kinases in gene regulatory networks. We have provided a list of possible new key regulators that could be further explored and also identified the role of hub proteins. The results of this study would be useful to develop new drug development.

Keywords: GeneMANIA, Microarray, NHEK, STRING, System Biology.

General Aspects of COVID-19 Pandemic: Useful Information for Pharmacists (Review)

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Introduction: Corona Virus 2019 (COVID19) was declared to be a novel contagious viral respiratory disease affecting the population of Wuhan, Hubei province, China on December 2019.it was first called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),but On February 12, 2020, WHO officially named the disease caused by the novel coronavirus as Coronavirus Disease 2019 (COVID-19).at first the morbidity was low but then as the number of infected patients increased, the number of countries struggling with COVID-19 outbreak increased as well and it was announced to be a global pandemic in need of extensive attention worldwide .although containment measures in China have reduced new cases by more than 90%, this is not the case elsewhere, and Iran is one of critical countries with more than 82211 reported cases and more than 5118 deaths until April 19th 2020 and it is not controlled yet and it is believed that this number is much more greater because a majority of patients experience mild symptoms and do not visit the doctor and another group are not tested with the diagnostic test kits so we can not say that they are positive and those who were contaminated with the virus but did not know due to lack of diagnostic methods and the delay in receiving diagnostic kits in Iran ,therefore these patients are not concluded in the statistics; seeing the statistics and understanding the crucial importance to overcome this pandemic , it is critical for the pharmacists to share information and enlighten the matter for the general population and other healthcare workers who ask about deferent aspects of COVID-19 because pharmacists play an important role as a link between doctors, health care providers and general population who people can trust to receive correct updated information. After knowing the corona virus, its diagnostics, its treatment and obtained information so far we can hope to find a cure and control the current corona virus crisis .

Methods: The article review was carried out between 2019 and 2020 following the outbreak of the novel COVID-19, inclusive using the following terms: coronavirus ,COVID-19,viral treatment and was preformed with usage of google scholar, Pubmed, Scopus, Elsevier, the lancet, world health organization guidelines, CDC and FDA websites and other similar data banks ,related to medical and pharmaceutical fields.

Results: By reviewing the literatures, a great source of information is provided regarding COVID-19 quiddity , structure , diagnoses, treatment and also further possible preventive, palliative and definitive therapy that are useful in managing this disease.

Conclusion: The more efforts scientists put in evaluating available information, the more closer we get to overcoming COVID-19 pandemic and this can be a lesson to prevent such catastrophic events and to be more prepared in future specially in

third world countries such as Iran that has limited resources and also with a strategic plan that considers all aspects of COVID-19 ,Iran can manage the disease, therefore less lives will be lost and it can gain financial profits economically.

Keywords: corona disease, covid-19, contagious viral disease, pandemic

Generated immune responses and antibody-mediated immunity against COVID-19 (Review)

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Introduction: The humoral immune system block the virus by producing antibodies. Viral load varies at different stages of the disease, the viral RiboNucleic Acid(RNA) test is likely to provide a false-negative result at the beginning of the disease and, as a result, these individuals, due to being a carrier, can spread the disease . it is probable that serological tests can identify suspected individuals by measuring antibody responses and thereby control the spread of infection. This study aimed to fill the knowledge gap in the human immune response to SARS-CoV-2 infection, which may contribute to identifying individuals with suspected COVID-19 to control the prevalence of the disease and to design an appropriate immunological intervention for the treatment, diagnosis, and development of prophylactic and therapeutic vaccines against COVID-19.

Methods: Article selection were conducted through advanced search in science direct, Pubmed database and without time limit, using two keywords derived from MeSH (Covid-19 and Humoral immune) and limiting the search to keywords in the abstract. From the 58 available articles based on the content of the abstracts, 16 articles to Humoral immune in COVID-19 were selected. The articles were studied and key points of each were identified.

Results: All types of lymphocytes including B cells (CD19 +), T cells (CD3+, CD4+, CD8+), and NK cells (CD16+, CD56) reduce in severe cases of the disease, but in normal condition, they are close to normal status and they increase after treatment with corticosteroids and antivirals. There is less CD19+ B cell in COVID-19-induced pneumonia than in non-COVID-19- induced pneumonia. Studies have shown that indicating that antibodies can be detected to achieve the early detection of COVID-19. IgM is an indicator of the acute phase & IgG is an indicator of the chronic stage of the disease. IgG and NLR responses can be applied as a complementary tool to differentiate between severe and non-severe COVID-19 patients. The results obtained from a study revealed that IgG antibody levels were higher in female patients at 2 to 4 weeks after the onset of the disease than in males. In elderly

patients, men report a higher mortality rate than women; female patients produce a more effective humoral response than men. Negative serological and positive molecular test results mean that individuals are infected but have not yet reached the phase of antibody production. Conversely, those who test positive on the serological test and negative on the molecular test may be at the recovery COVID-19 phase or inappropriate sample collection. Antibody detection kits have several advantages over RT-PCRs: they are time-saving techniques, do not require special equipment, they are simple to apply, they require minimal training, capability to perform this screening test for asymptomatic patients is another application of such tests. Furthermore, there are some false positives caused by the interference of developing other diseases such as autoimmune diseases and other infections as well. The results suggest that high levels of NAb are useful for viral clearness and elderly patient recovery. convalescent plasma(CP) may be effective but also increases the risk of developing antibody-dependent enhancement(ADE). ADE can interfere with vaccine efficacy since the vaccine may produce antibodies that cause the disease to be exacerbated.

Conclusion: In this study, humoral immune responses and antibody production program in patients with COVID-19 were reviewed. Given that the identification of individuals suspected of having SARS-CoV-2 infection is of great importance in terms of controlling the prevalence of the disease and it may help determining the immune stability due to antibodies after recovery; further extensive research is required. It can also develop a broader vision of vaccines stimulating the humoral immune system.

Keywords: Humoral immune, Antibody, Seropositive, COVID-19, SARS-CoV-2

Generation of GMP-grade human induced pluripotent stem cells (Review)

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Introduction: Stem cells (SCs) classified into two essential groups based on their plasticity and sources. Adult stem cells and embryonic stem cells (ESCs) (Inner cell mass of mammalian blastocysts) are two primary sources that naturally existing in body of human. Moreover, in 2006 the third SC sources announced by Yamanaka and Takashi via genetic manipulation. Induced pluripotent stem (iPS) is an artificial stem cell that has been discovered by overexpression of three or four factors (Oct4, Klf4, Sox2, and [c-Myc or l-Myc]) that highly expressed in ESC or Thomson 4 factors (Sox2, Oct3/4, Nanog, and Ln28) and reprogrammed mouse and human somatic cells. However, iPS cells have essential characteristics of ESCs such as normal karyotypes, telomerase activity, maintain the ability to differentiate into all three germ layers, moreover they have same genes and cell surface markers. After that, some groups had investigated the procedure of Yamanaka with other mouse tissues for verification and validation. Even, human differentiated cells could have successfully reprogrammed toward iPS cells. But the most important reason for its expanded studies and usage is personalized medicine means generating iPS cells from the patients' own cells that remove immune rejection by recipient and ethical difficulties regarding the use of the human embryo. This unlimited source of cells has been exploiting for many disease modeling, toxicology assays, drug screening and discovery in the comprehensive field of regenerative medicine. Presenting proto-oncogenes (C-MYC and KLF4) into the Yamanaka method and better understanding of molecular mechanism of pluripotency have been persuading scientists to consider different strategies that have more safety and efficiency. Although, c-Myc has been identified as a dispensable factor for reprogramming, absence in this procedure intensive affects efficiency. Retro and lentiviruses are the first vehicles that have been used in reprogramming, but because of oncogenic activation by reason of integration into host genome, subsequently low safety, their clinical application have been abolished, however have still the highest reprogramming efficiency. Recently, In order to safe, clinical-grade and GMP (good manufacturing practice) manufacturing, integration-free and non-viral methods have been preferring for generation of iPS, such as using episomal plasmid vector, synthesized mRNA, microRNA, Sendai virus, recombinant proteins, small molecules. Also, several studies have accomplished in investigating a safe and effective method in clinical application. But these strategies need to be continued for further scrutiny.

Methods: Reprogramming factors such as DNA, mRNA, miRNA, protein, and small molecules have been delivering by integration or non-integration methods. Integration methods are including Retro and lentiviruses, that have the possibility of tumorigenicity. Various types of non-integration methods classified into two groups based on virus usage: 1/viral approaches (adenovirus, sendai virus (SeV)), 2/Non-viral approaches (plasmid transfection, piggy Bac transposon, minicircle vector, episomal plasmid, modified mRNA, self-replication RNA (srRNA), micro RNAs, xeno-free condition, recombinant proteins, and small molecules. Also, chemical and physical methods have established for reprogramming process.

Results: The integration method that at first step had used for the generation of iPS cells is not a safety method, although high efficiency. Thus, this method is currently used for drug discovery and disease modeling. Scientists are leading to a new non-integration strategy with high efficiency and safety for clinical application.

Conclusion: Biophysical and biochemical factors are prompting for cell reprogramming. For example, extracellular matrix forces variation, 3D microenvironment, nanoparticles, and 3D scaffold coated with growth factors and small molecules. Studies are continued and need to consider in GMP grade iPS generation.

Keywords: iPS, cell reprogramming, nanotechnology, biomaterial

Glycyrrhizin and antiviral effect on Covid-19 (Review)

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Introduction: Glycyrrhizin is a pentacyclic triterpenoid saponins glycoside obtained from the root and stolons of the plant Glycyrrhiza glabra. Glycyrrhizin is used worldwide as a natural sweetener and flavoring additive. But its medical uses is more important.

Methods: It has antiviral activity against various DNA and RNA viruses, including HIV and severe acute respiratory syndrome (SARS) associated corona virus.At this article we want to talk about the effect of glycyrrhizin on the corona virus. The coronavirus, which spread from China, and it has spread quickly nationwide and causing severe respiratory problems.

Results: The ACE2 or angiotensin converting enzyme 2 is a receptor that corona virus uses it and entry into target cells, which is recognized by epithelial cells of the lung, intestine, kidney and blood cells.

Conclusion: Glycyrrhizin has been shown to have the potential to bind to ACE2 That less ACE2 is available to the coronavirus. And if glycyrrhizin used in the early stage of this disease can attenuate excessive cytokine storms that cause acute respiratory distress syndrome and septic shock in patients with COVID-19. The reactive oxygen species or ROS accumulate in the inflammatory response that glycyrrhizin inhibit the accumulation of them besides that glycyrrhizin can reduce the replication of virus with the reduce activation of nuclear factor kappa beta(NFkB) ,c-Jun N-terminal kinase(JNK),p38. According to studies and research glycyrrhizin may also have a role in treatment of COVID-19 indirectly.

Keywords: Glycyrrhizin, COVID-19, ACE2

Green space and preterm birth: A systematic review study (Review)

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Introduction: Introduction: The impact of the environment on reproductive health and pregnancy outcomes has been expressed in a number of epidemiological studies. Exposure to green space has been shown to improve health as well as improve fetal growth and reduce the risk of pregnancy complications. In the present study, we conducted a systematic review of all relevant studies with the aim of investigating the relationship between green space and preterm delivery.

Methods: Method: In this study, a review was conducted to obtain relevant studies from the English databases Pubmed, Scopus, Web of science and Persian databases Iran Medex, SID and Magiran with the English and Persian keywords green space and preterm birth with all possible search combinations.

Results: Results: Out of 6964 articles, 14 articles (10 cross-sectional studies and 4 cohort studies) were included in the study criteria. In the qualitative evaluation of articles with STROBE index, 10 studies were of high quality and 4 studies were of medium quality. In general, in these studies, green space exposure was evaluated with normalized indices of vegetation difference (NDVI), proximity to green space and distance to parks and recreational facilities. The results of most studies showed that there was no relationship between green space and preterm birth, and the rest of the studies expressed conflicting results on the protective effect of green space on preterm birth.

Conclusion: Conclusion: The results of most studies showed no association between green space and preterm birth and gestational age. While a number of studies have reported conflicting results on the protective effect of green space on preterm birth. Therefore, it is suggested that further studies be conducted in this area.

Keywords: Keywords: green space, preterm birth, gestational age

Health literacy and breast cancer (Review)

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Introduction: Health literacy is a broad concept defined in a variety of ways. Health literacy is the capacity for acquisition, processing, understanding of information and basic services for appropriate health decisions. Health literacy is heavily important for breast cancer patients so that therapists can decide on a complex set of decision-making decisions based on diagnosis and treatment when physical and emotional distress. Breast cancer is the most common cancer among women throughout the world. Considering the effect of this disease and its treatment on different dimensions of life, evaluating the level of health literacy of patients in order to improve their health seems useful before any study.

Methods: This study was conducted with the aim of reviewing the world literature on health literacy and breast cancer. In this systematic study, the terms health literacy and Breath Cancer were searched in the title and abstract of the articles published in internationally recognized scientific databases and all English and related articles were listed.

Results: Then the abstract of the articles was examined and in several stages repeated and unrelated items were excluded from the study. Finally, the final papers were selected for comprehensive review and data extraction.

Conclusion: The overall result of this study was that according to the literature reviewed, literacy can have an impact on the prevention of breast cancer and the management of symptoms resulting from the disease.

Keywords: Health Literacy breast cancer Regular Review Women

Health of Hygiene, Prevention and Treatment Health Services Clinic and Referral Corona Patients New Virus ((nCOVID_2019 (Review)

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Introduction: Background and Purpose; Coronavirus (COV) is a large family of viruses that causes common illnesses such as colds to respiratory illnesses such as Middle East Respiratory Syndrome (MERS_COV) and Acute Respiratory Syndrome (SARS_COV). The unprecedented launch of the Coronavirus in the Chinese city of Wuhan in December 2019 revealed that COVID-19 is a beta coronavirus. The goal is to assess the health of hygiene, prevention and treatment of clinical services and referral of new coronavirus patients.

Methods: materials and methods; In this review study, all articles published in 2020 in English on new Coronavirus infection were reviewed. There are also reputable health websites in the world, such as the World Health Organization and the Centers for Disease Control and Prevention (searched in PubMed, Scopus, Google scholar databases) and used to obtain the latest statistics and information on the disease. Clinical features, methods of transmission, treatment and prevention of this disease have been extracted from the above articles and websites.

Results: findings; The mortality rate of this virus is significantly higher in the elderly and people with underlying diseases than in healthy people. High-risk groups for this disease include cardiovascular, diabetic, chronically ill, and hypertensive patients, respectively. The mortality rate in healthy people is estimated at less than one percent.

Conclusion: Conclusion; The new Coronavirus Pandemic is more widespread in humans than previous Coronaviruses, which indicates the high potential for highly contagious transmission of the virus. Currently, due to the lack of effective treatment and vaccines, the best way to deal with this disease is to avoid contamination and prevent its spread through protective measures and personal hygiene.

Keywords: Keywords: Corona new virus, health of hygiene, prevention, treatment, clinical services.

Heat shock proteins in patients with type 2 diabetes (Review)

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Introduction: Heat shock proteins (HSP) are a large family of proteins that are expressed in response to various types of stresses. Many studies have confirmed the association of these proteins, especially the HSP70 family; with type 2 diabetes.

Methods: In this manuscript, based on studies and researches; at the first the structure and function of HSP70 was explained. The factors involved in diabetes (apoptosis, inflammatory, oxidative stress, insulin resistance, and defect in its signaling pathways) and their associations with HSPs were discussed. Then some explanations will be given about type 2 diabetes, especially its association with cancer diseases. HSP levels in patients with type 2 diabetes and its association with the duration of the disease are compared with healthy controls.

Results: The conserved structure of heat shock proteins plays an important role in their importance and that these types of chaperones could be targets for extensive studies in relation to various diseases. In this article, based on a review of various studies and researches, it has been proven that between the causes of type 2 diabetes such as inflammation, oxidative stress, insulin resistance or signaling defects, and the level of heat shock proteins, especially HSP70 There is an obvious link. In addition, the level of HSP70 chaperones is directly related to the duration of the disease.

Conclusion: Form various studies and researches, it will be concluded that the HSP70 levels are higher in patients with type 2 diabetes and in patients with longer duration of disease compared with healthy control.

Keywords: Heat shock proteins - HSP70- diabetes- Oxidative stress

Histopathological evaluation of different doses of Nickel on female Wistar rat kidney (Research Paper)

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Introduction: In recent years, many investigations have been carried out on Nickel, the widespread toxic metal throughout the environment. Although humankind could encounter Nickel occupationally, general populations are mainly exposed to Nickel by air, water and food. Hence, people can get contaminated by Nickel through nutrition. So far, numerous studies have illustrated toxic and carcinogenic effects of Nickel on animals as well as humans.

Methods: 32 female Wistar rats were split into 4 groups evenly. The duration of test was 20 days. Control group received nothing but water intraperitoneally. Nickel was given to three other groups by intraperitoneal injection alternatively by doses of 10, 15 and 25mg/kg, each thrice on days 8, 12 and 16 of the examination. On day 20, rats were sacrificed after general anesthesia administration by Ketamine and Xylazine. Then, kidney specimens were obtained for hematoxylin and eosin staining and ultimately, histopathology sections have been prepared.

Results: Whilst Control group indicated normal kidneys, Nickel treated groups have showed numerous pathology lesions including infiltration of inflammatory cells, hyperemia and vacuolar degeneration, whose intensity gets much severer by increasing dose of Nickel and also, the dose 25mg/kg illustrated the worst pathological condition amongst all groups.

Conclusion: According to histopathology sections, it can be concluded that Nickel has adverse impacts on kidney.

Keywords: Nickel, Histopathology, Kidney, Wistar rat

How can nutrition help to prevent and cope with coronavirus disease? (Review)

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1.
2.

Introduction: At the time of this writing, COVID-19 infection has taken the lives of more than 876,000 individuals worldwide. This pathogenic virus causes an acute respiratory syndrome that spreads rapidly around the world. No vaccine has been discovered for it so far, and the control ways include case isolation, identification, and follow-up of contacts, environmental disinfection, use of personal protective equipment, and amplification of the immune system. A well-function immune system needs several vitamins and essential nutrients. A proper diet can make sure that the body can resist the virus.

Methods: we conduct a comprehensive search in Google Scholar, Pub Med databases for meta-analysis, RCT, review articles.

Results: All the articles check out the role of vitamins and minerals in augmenting immunity. Vitamin A has an essential role in gene expression and immune cell maturation. Adequate intake of vitamin A can improve the symptoms of acute pneumonia. Vitamin B group deficiency, especially B12, B6, and B9, decrease phagocyte action and T, B lymphocyte cells. Vitamin C can improve antibody production and natural killer cells in lymphocyte activity. Vitamins C and E are antioxidants too. Vitamins D and E deficiency increase in susceptibility respiratory tract infection. Adequate zinc levels reduced mortality during severe pneumonia because zinc deficiency decreased natural killer cell activity and lymphocyte proliferation. Copper plays an important role in immunity development against respiratory viruses. The body needs iron for maturation and proliferation of lymphocytes. Selenium battle against oxidative stress in viral infection.

Conclusion: The immune system protects our body from pathogens. A rich diet that includes vegetables and fruits can help us to achieve a healthy life without illness. However, the definitive's effect of vitamins and minerals has been not proven in COVID-19, but they are necessary for the immune system.

Keywords: COVID-19, immune system, vitamin, mineral

Human corneal shape prediction with mathematical tools (Research Paper)

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Introduction: The eye is one of the most vital organs in the human body. The protective envelope of the eye that covers the iris, pupil, and the anterior chamber is the cornea. It is the most transparent tissue and responsible for the optical system well-functioning [1]. In certain diseases, the corneal geometry may alter so accurate construction of the corneal shape can assist in the early detection of certain conditions. For example, the corneal topography is abnormal in astigmatism, hyperopia, keratoconus, and myopia. Additionally, corneal shape prediction can be helpful for lens design. Recently, a nonlinear two-point boundary value equation was developed for human corneal shape based on physical motivation [2]. The solution of the corneal equation, predict the corneal shape. For some special conditions, the corneal equation has been solved using different methods [2-4]. In this work, we propose a simple approach to solve the human corneal shape equation that includes all real conditions correspond to the normal and abnormal cornea. The accuracy and convergence of the presented solutions are evaluated for various cases.

Methods: A dimensionless nonlinear differential equation proposed for the human corneal shape is [2]: u^'' (x)-a u(x)=-b/√(1+〖u^' (x)〗^2). u^' (0)=0. u(1)=0. (1) where a and b are positive constants as a = KR2/T and b = PR/T. K is the elasticity coefficient, R is the radius of the cornea, T is the corneal surface tension, and P is intraocular pressure. The nonlinear term, 1/√(1+〖u^' (x)〗^2), is the major challenge in solving Eq. (1). Using different assumptions, three accurate approximate analytical solutions are developed for Eq. (1) that are Approximation1, Approximation 2, and Approximation 3. In the following juts, the method of solving in Approximation1 is presented and the others are addressed in the appendixes. In Approximation1, it is assumed that |u^' (x)|<1, and then the finite Maclaurin expansion is applied for the nonlinear term. u_0^' (x) is approximated by the zero-order solution [3] or linear solution and combining the homogeneous and particular solutions, and incorporating the boundary conditions, an analytical approximation solution of Eq. (1), is developed as follows: u(x)=∑_(m=0)^N▒〖C_2m cosh⁡(2mαx)-(∑_(m=0)^N▒〖C_2m cosh⁡(2mα)〗) cosh⁡〖(αx)〗/cosh⁡〖(α)〗〗 . (2) For N=2 as an example, the solution of the corneal equation is obtained as follow: u(x)=〖C_0+C〗_2 cosh⁡〖(2αx)+C_4 cosh⁡(4αx)〗-[〖C_0+C〗_2 cosh⁡〖(2α)+C_4 cosh⁡(4α)〗] cosh⁡(αx)/cosh⁡(α) . (3) Huge mathematical computation is applied to solve the equation that is not presented here. There is no need to deal with physicians with mathematical computations. By plotting u(x) the corneal shape is obtained which is helpful for eye researchers.

Results: Having a and b which are measured clinically, and differ from person to person, the corneal shape is plotted by u(x). Three cases are selected to validate the proposed solutions at weak, moderate and strong nonlinear conditions. They

are, respectively, Case 1: a=2.0, b=0.5, Case 2: a=1.7, b=1.6, and Case 3: a=0.5, b=2. Case 1 represents low intraocular eye fluid pressure caused by Hypotony, Case 2 represents typical cornea [2, 3], and Case 3 represents high intraocular pressure caused by keratoconus. Fig. 2 compares the curve of u(x), the corneal shape, obtained by the proposed solutions, the numerical solution, and the other closed-form solutions [3, 4] for Case 2 and N=2. The results of the Approximation 1 and 2 are in excellent agreement with the numerical results, and they are more accurate than the other closed-form solutions [3, 4]. However, there are significant discrepancies between the results of Approximation 3 and numerical results. Fig. 3 shows the comparison between the results for Case 1 and 3.

Conclusion: The human corneal shape is obtained by solving the human corneal equation. The obtained results are valuable and practical in diagnostic purposes, early detection, custom lens design, and refractive surgery. The presented solutions are not only simple and easy to use but also more accurate than the other available solution in the literature. In contrast to the numerical solution, our approximate analytical solutions can identify the effect of determinant parameters in the corneal performance, which is helpful in ophthalmology.

Keywords: Human corneal shape, early detection, lens design, Nonlinear ordinary differential equation

Human Epidermal Growth Factor Receptor-2 Assessment in Cancerous and Precancerous Lesions of the Stomach in Presence of Helicobacter Pylori (Research Paper)

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Introduction: Importance of Human Epidermal Growth Factor Receptor-2 (HER-2) testing in cancer is increasing and on the other hand the there is a hypothesis about the role of Helicobacter pylori (H. pylori) in gastric cancer (GC) development. We seek to investigate the HER-2 expression in the presence of H. pylori infection in patients with gastric GC and precancerous lesions.

Methods: From 224 archived blocks, 58 samples with chronic gastritis, 58 intestinal metaplasia (IM), 58 gastric dysplasia and 50 gastric adenocarcinoma cases were selected as our principal groups. Each group was subdivided into H. pylori-positive and negative subgroups. The immunohistochemical method was performed for the detection of HER-2 expression in gastric biopsies using a polyclonal antibody. The staining intensity was quantified and differences among groups were compared using Mann-Whitney U and Kruskal-Wallis tests. P values less than 0.05 was set as significant.

Results: Results showed that HER-2 expression among the four principal groups was statistically significant ($P<0.05$). There was a significant Increase of immunohistochemical expression of HER-2 in H. pylori-positive chronic gastritis compared to H. pylori-negative subgroup ($P<0.05$). The difference of HER-2 expression between H. pylori-positive and H. pylori-negative subgroups in dysplasia, IM and GC groups was not statistically significant ($P>0.05$).

Conclusion: The present study proposed that HER-2 overexpression in gastric tissues probably had important roles in the progression of cancer and the mentioned process probably was associated with H. pylori infection in the early stages of the precancerous lesions.

Keywords: Adenocarcinoma; HER-2; Gastric cancer; Gastritis; Helicobacter pylori.

Hydrogel nanoparticles in drug delivery (Review)

Mohammad Reza Salehi Kia,[1,*]

1.

Introduction: Hydrogels are hydrophilic three-dimensional networks. They have cross links which swell in contact with water without being solved. These compounds can have different forms such as slab, microparticle, nanoparticle, coating structure, and film. Due to different forms, hydrogels can be used in different fields of research including biosensors, tissue engineering, separation of biomolecules or cells, and regulation of bioadhesion of materials. Materials which have hydrogel nanoparticle structure, represent the characteristics of both hydrogels and nanoparticle simultaneously. Hydrogel nanoparticles have many applications. The most important application them is cellular-target therapy. In addition, they can be used in controlled releae of proteins such as Lysozyme, Albumin, and Immunoglobulin.

Methods: This study is a library research. It seeks to collect general information and scientific researches on hydrogels.

Results: Hydrogels are polymeric networks with three-dimensional structures which can absorb a lot of water or bioliquides because of existence of hydrophilic groups like hydroxid in polymers which form the structurr of hydrogel. The gel will be hydrate in terms of the nature of water environment and the structure of polymer and it can be reach more than ninety percent by weight of the polymer. Water content of hydrogels plays a pivotal role in determination of the whole characteristics of polymeric network. Therefore, they have distinctive features which differentiate them from hydrophobe polymeric networks. It is worth mentioning that the preparation of hydrogels is significantly milder and in addition to gel formation at ambient temperature, organic solvents are rarely used in their production process. Hydrogels, especially those used in biomedicine and drug delivery, must have acceptable biocompatibility and biodegradability. The structure of the hydrogel network can be macroporous, microporous, or nonporous. Macroporous hydrogels have large pores in the dimensions of 1, 0, up to 1 micrometer. These hydrogels release the drug trapped inside their pores through a mechanism which depends on the drug diffusion coefficent. Microporous hydrogels have small pores in the demension of 10 up to 100 nanometer. They release the drug trapped inside their pores through diffusion processes and molecular convection flow. Nonporous hydrogels are consisted of seive-like structures in the demensions of macromolecules with pores of 1 up to 10 nanometer which are formed by making cross links in monomeric chains. In these structures, drug release occurs only through the diffusion mechanism.

Conclusion: Hydrogel-based drug delivery, among different applications of hydrogels, has gained significant attention. It is a field in progress. Obvoiusly hydrogels can protect drug from internal destructive factors such as enzymes and PH changes. Their porosity causes drug loading in gel matrix and their release with predetermined speed. Encouraging applications of hydrogels in the fields of

medicine and pharmacy include materials controlling enzyme activity, destabilizing factors of double layer phospholipids, materials controlling reversible cell-binding, nanoreactors with the possibility of accurate inclusion of active groups in three-dimensional space, intelligent microfluids with responsive hydrogels, and energy conversion systems.

Keywords: nanoparticles, hydrogel nanoparticles, drug delivery, medicine, polymer

Hypertention and Dementia appearing in elderly people : A systematic review (Review)

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Introduction: Introduction: nowadays the phenomenon of aging is taken into consideration because of the Life expentancy elevation and elderly have the fastest population growth rate among different age groups. Due to the increasing prevalence of chronic diseases in the elderly, these people need more health and social care than other citizens of the community. Dementia is one of the most common chronic disorders with severe and progressive disability in the elderly. If no recent treatment and prevention methods are found, it could become a widespread epidemic in the world in the next few years. The purpose of this systematic study was to determine the effect of Hypertension on Dementia in the elderly.

Methods: Metods: In this study, which is a systematic review, by reviewing authoritative books, related materials and concepts, collected and categorized and searched in selected scientific databases, including Iran medex, Google Scholar, Pubmed, SID with the keywords elderly, Dementia , Cardiovascular disease, risk factor, hypertension, complication were used and 350 articles were obtained. Among these articles, the full-text articles that were available and published in the last five years received further scrutiny.

Results: Results : The results of this study represents that Hypertention is one of the major causes of Dementia in the elderly. Thus, Hypertention causes atherosclerosis in the blood vessels and hypoperfusion of brain tissue, causing problems in the brain and weakening, shrinking and atrophy the brain tissue and this factor can lead the elderly to dementia.

Conclusion: Conclusion: The results of this study represents that there is a close relation between hypertension and dementia in the elderly; Therefore, it can be expected that by performing timely medical interventions and controlling blood pressure in the elderly, the incidence and severity of dementia in these people will be reduced. Preventive measures require intervention in screening, timely identification, treatment, education and proper information. To improve lifestyles, people can change their performance by increasing their awareness through mass media. Awareness of the real needs and demands of the elderly's health is an

important step not only for managers, but also for family members, to prevent disease and disorder, protect and promote the health of the elderly.

Keywords: Keywords: Cardiovascular disease, hypertension, dementia, risk factor, elderly

Identification and interaction analysis of hub genes and microRNA in hepatocellular carcinoma: using integrated bioinformatics analysis (Research Paper)

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Introduction: Hepatocellular carcinoma is considered about 90% of liver cancers, which is being caused by hepatitis B and C viruses named HBV and HCV respectively. During the last decades' researches, the molecular mechanisms of HCC is still under study. Based on the latest studies, different risk factors could trigger HCC, which among them the genetic biomarkers such as miRNAs (small non-coding RNAs) are considered to have essential impact on HCC progression. Thus, a wide range of bioinformatics analysis have been used for the recognition of these biomarkers as promising targets for the diagnosis and treatment of HCC.

Methods: Initially, NCBI Gene Expression Omnibus (GEO) has been chosen to get the essential GSE, which this gene expression profile has been downloaded and analyzed by R studio in order to find the genes which have notable up and down expression regulations, that by analyzation of genes' pathways, RRM2 has been selected. Moreover, miRWalk and miRTarBase databases have been used to identify numerous target microRNAs of RRM2. The binding and paring scores of these microRNAs have been studied which the interaction of them have been showed as a Cystoscope software (3.8.0). Eventually, the analyzation of the pathways involved in HCC, the required microRNA has been selected.

Results: Based on GEO analysis total number of 2 GSEs were indicated among HCC and cirrhotic tissues. This analysis outcomes assigned that the GSE112790 and GSE121248 were surprisingly enriched in several biological mechanisms. A total number of 29 up-regulated and 100 down-regulated genes from both GSEs were indicated which by DAVID database the pathways of each were examined separately. Up-regulated genes pointed HCC-related pathways named, cell cycle and p53 signaling pathways that RRM2 demonstrated as a vital gene of these pathways. Moreover, 100 DEGs were revealed to be included in both pathways with significant downregulation of expression.

Conclusion: According to the all mentioned events, concluded that hsa-miR-34a-5p via inhibition of RRM2 gene's function, an essential gene for cell growth, acts as tumor suppressor in p53 signaling pathway of HCC. Thus, these findings could provide a promising therapy method for treatment of HCC patients.

Keywords: Liver disease, Hepatocellular carcinoma, Bioinformatics, miRNA, pathway

Identification and role of ETEC by real time PCR in a sample collected from patients with IBD (Research Paper)

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1.

Introduction: Inflammatory bowel disease is a common and lifelong gastrointestinal disease. A number of cult-based studies and molecular methods have shown that Escherichia coli bacteria can play a role in IBD. Therefore, the aim of the study was to investigate the relationship between IBD and bacterial leishmaniosis (ETEC) in relation to IBD and non-IBD

Methods: In this cross-sectional study, 81 paraffin blocks including 41 positive IBD samples and 40 control samples (healthy) were examined for ETEC bacteria. Samples were collected from Ghaem Hospital between 2016 and 2016. Initially, the blocks were cut to extract DNA and the DNA was extracted manually. Then, the design of the private premium probe for ETEC identification was done by Real Time PCR method. After confirming the primers, Taqman prob Realtime PCR was performed on IBD and control sample.

Results: DNA extraction was performed and its quality was confirmed by nanoparticle device. Demographic results showed that the mean age of IBD and control patients was 51 and 46, respectively. The results from Real Time PCR showed that 12 cases (30%) of IBD-positive individuals were positive for ETEC, while no positive cases were observed in control individuals (negative IBD). Statistical study shows that there is a statistically significant difference between the two groups in terms of ETEC bacteria.

Conclusion: Given the conditions of IBD and the results of this study, the presence of the toxin bacterium Escherichia coli is likely to exacerbate the conditions and symptoms of IBD by producing toxin virulence factors.

Keywords: (IBD): Inflammatory bowel disease (ETEC): Enterotoxigenic Escherichia coli

Identification of a novel mutation in the SDCCAG8 gene in an Iranian family with Bardet-Biedl Syndrome (Research Paper)

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Introduction: Bardet–Biedl syndrome is known as a rare ciliopathic human genetic disorder. Typically, BBS follows the autosomal recessive pattern of inheritance, however, it has also been reported as an oligogenic inheritance. The prevalence of BBS among the populations varies from 1 in 13500 to 1 in 160000. BBS is a genetically heterogeneous disorder with a wide spectrum of clinical manifestations including loss of vision, obesity, extra fingers or toes abnormalities of the genitalia, intellectual disability, and several other features that make its diagnosis and management more challenging. RetNet reports 18 genes that cause BBS and each of these genes has had numerous known mutations. Genetic studies suggesting that SDCCAG8 (also called BBS16) gene mutations are a major cause of BBS. This gene plays an essential role in the formation of cell polarity, epithelial lumen, and ciliogenesis and is also a prominent element in the Hedgehog signaling pathway.

Methods: In this section, we investigated the consanguineous Iranian family members with BBS. Whole-exome sequencing (WES) and Sanger sequencing, were performed to screen and confirm the suspicious pathogenic mutations. The identified mutation was investigated using bioinformatics tools to predict the effect of the mutation on protein structure.

Results: The sequential analysis revealed a novel splice site mutation c.1221+2 T>A in the SDCCAG8 gene in BBS patients. Structure-based approaches have predicted significant structural alterations in SDCCAG8 protein.

Conclusion: This study was conducted to show the aberrant alternative splicing as one of the single splicing mutations identified can cause BBS by affecting the function of SDCCAG8 protein.

Keywords: Bardet–Biedl syndrome (BBS); SDCCAG8; Whole-exome sequencing; Novel mutation, Bioinformatics

Identification of common SNPs in the chromosome 11region: from 12,535,356 to 12,377,571 (Research Paper)

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Introduction: Nowaday , with the development of bioinformatics, it is possible to diagnose and treat many diseases . For example, snp can be identified by using bioinformatics. SNP or single nucleotide polymorphism is one of the factors of phenotypic change within a species and it is considered as an important genetic marker. SNPs can affect a person's risk of developing cancer. There are several bioinformatics tools for identifying SNP. One of these sites is the galaxy bioinformatics site . This program allows researchers to perform bioinformatics work and analysis without the need to use coding. The aim of this study was to identify the most common types of SNP in a part of the chromosome 11 region: from 12,535,356 to 12,377,571

Methods: 1-First, the coding sequences data of the desired area was extracted from the ucsc site with the ncbi refseq source and loaded on the galaxy site. 2-Then, the SNP sequences data of the whole genome in the desired region were extracted from the ucsc site 3-After that, we joined the two extracted data together 4-Using the statistic option on the galaxy site on the joined data, the count operation was performed and then sorted 5- Finally, we compared the obtained data with the initial data of the coding of the desired area

Results: The extracted coding data had 26 regions and the extracted SNP data had 34,617 regions. After merging the two extracted data, the data with 698 regions was created. This data indicates the amount of overlapping between exons and SNP. After counting, the data with 26 lines was obtained, which shows the number of SNP for each exon. By sorting the data, they are sorted based on the maximum amount of SNP for each exon. Compared to the sorted data with the initial coding data, 25 exons were classified based on the highest SNP value. The highest density was 46 in the target area.

Conclusion: In the chromosome 11 region: from 12,535,356 to 12,377,571, the PARVA gene is located .The PARVA gene is one of the oncogenes of lung cancer and can induce VEGF expression. Also the VEGF gene is involved in the cancer angiogenesis process. Therefore, recognizing common SNPs of PARVA genes can be important and provide a way to identify or treat cancer. Also, by laboratory examination of these SNPs and genetic manipulation of them , we can better understand the mechanism of cancer

Keywords: SNP, CANCER. BIOINFORMATICS

Identification of Key Genes in Pancreatic Ductal Adenocarcinoma Gene Expression Profile by Integrative Analysis (Research Paper)

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Introduction: Among all of the cancer types, beyond one-quarter is considered as the gastrointestinal ones. Pancreatic cancer is rated as the 7th mortal cancer globally. With a median survival of 6 months or less, Pancreatic ductal adenocarcinoma (PDAC) (an exocrine tumor) the fourth lethal malignancy in developed countries. With a median of 6 months or less, PDAC is the fourth lethal malignancy in developed countries. The aggressive nature of the tumor, which discomfits its diagnosis, chemotherapy and radiotherapy resistance, and moreover the poor specificity and sensitivity of PDAC's biomarkers (CA19-9, the sole biomarker in the clinical investigations) are the current challenges in this illness. There is a bright outlook on the development in diagnosis, therapeutic, and prognosis of PDAC, based on biological improvement and integrated bioinformatics analysis In this study, we aim to collect all of the microarray data related to PDAC's gene expression by bioinformatics appliances, and analysis the GSE data downloaded from the NCBI GEO database. We draw a protein-protein interaction network (PPI) to evaluate up regulations and down regulations the gene expression of coding genes to perform pathway analysis as an attempt to respond the mentioned challenges.

Methods: datasets of pancreatic ductal adenocarcinoma were searched using the keywords: 'pancreatic ductal adenocarcinoma, 'Homo sapiens' and 'Expression profiling by array' against the Gene Expression Omnibus (GEO) database (http://www.ncbi.nlm.nih.gov/geo). To identify differentially expressed genes (DEGs), each dataset was analyzed by limma R package in Bio conductor. Significant differential expression was determined as a log fold change ≥ |1| and adjusted p-value threshold of 0.05. to find the correlation between collected genes, draw Protein-Protein Interaction network (PPI) and report the hub genes.

Results: After a systematic review, seven GSE profiles from 34 datasets (GSE102238, GSE46234, GSE63111, GSE78229, GSE89997, GSE62452) which include 315 cases, were included. To the evaluated quality of data. Heat map and principle Component Analysis (PCA) was performed.

Conclusion: Based on PPI networks, top 10 DEGS such as ATM, BRCA2, MSH2, PTEN with high Degree and Between collected AND Pathway analysis were performed.

Keywords: keyword : pancreatic ductal adenocarcinoma, Gene expression, insilico

Identification Of Plasmodium By Aptamer-based Biosensors And Their Treatment By Mesenchymal Stem Cells (Review)

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Introduction: Malaria is recognized as a dangerous and long-standing infectious disease caused by pathogen named Plasmodium in the scientific community. There are several ways to identify the biological agents that cause malaria, but one of the newest scientific methods used is biosensors. Biosensors are one of the newest methods in identifying diseases and pathogens early and these biosensors have advantages such as the speed of detection, high accuracy and etc. On the other hand, in the field of treatment of this parasitic disease, we are facing problems such as reducing the effectiveness of common drugs to overcome this problem, various treatment methods have been proposed, one of which is the use of stem cells. Stem cells with high potential in medical science and treatment of diseases have been studied for microbial-based diseases (1-3). The purpose of this study was to investigate the potential of biosensors and mesenchymal stem cells to detect and treat plasmodium as a novel therapeutic approach to counteract antibiotic resistance.

Methods: Articles related to keywords such as plasmodium, a new therapeutic approach, aptamer-based biosensors, and mesenchymal stem cells, which were published have been extracted and used.

Results: Aptamer-based biosensors begin to identify based on their molecular structure and genome form and some specific peptides. One of the most well-known aptamers that have ever been studied is named 2008s have identified a specific loop connections which is created by Plasmodium Falciparum and does not exist in healthy body cells. For example, studies on the therapeutic properties of mesenchymal stem cells (MSCs) on malaria specimens have generally reported positive results. By injecting MSCs into mice infected with Plasmodium, the immune system of mice increased substantially, so that after the injection of stem cells, the rate of IL- 2 and 12 increased in these samples and they could fight against with Plasmodium by enhancement of the immune system On the other hand, these cells reduce the production of IL-10. The results of study can be related to the injection of MSCs and their effect on the body of specimens and various factors such as the amount of resistance and susceptibility of the host to this infection and genetic factors .

Conclusion: With the advancement of pathogenic factors and microbes, including bacteria, parasites, etc., medical science and treatment must multiply the speed of its development many times over these pathogens, as it is today. Designing and implementing new identification and treatment methods, such as the brief review in this article, can be one of the most effective methods. Biosensors should be used in a variety of situations because of the benefits, speed and accuracy. The use of stem cells on laboratory samples has so far been reported with a very positive

overall result but further studies should be conducted to investigate the various factors that may influence this treatment.

Keywords: Plasmodium, Aptamer-based biosensors, Mesenchymal stem cells.

Immunological communication between SARS-CoV-2 and dipeptidyl peptidase- 4: a possible therapeutic strategy. (Review)

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Introduction: Coronavirus disease 2019 (COVID-19) is a severe global pandemic and a new form of coronavirus, named SARS-CoV-2. Although it has many common symptoms such as tiredness, dry cough and fever, this illness appears to perform differently in many ways and symptoms form a person to others. Recent reports express that elder sufferers with previous illness, like diabetes, were at superior danger for mortality and COVID-19. One of the risk factors for SARS-CoV-2 infection in sufferers with diabetes is high blood glucose stage due to hyperglycemic hormones.

Methods: Dipeptidyl peptidase- 4 (DPP-4) also named as adenosine deaminase binding protein or CD26, is a major protein implicated for the action of a catalyst by enzymatic activity and binder for proteins and ligands. It exists both on the cell membrane and soluble in plasma and is expressed in epithelial and endothelial cells, such as blood vessels, mucosal glands, pancreas and T cells.

Results: DPP-4 directly influences glucose levels and homeostasis, which increases the development of metabolic diseases. DPP-4 is also in charge of decreasing insulin secretion and metabolism of adipose tissue by degradation of incretins, such as glucagon like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptides. These processes happen when food containing glucose is consumed. Furthermore, DPP-4 is associated with many immunological functions, such as modulating NF-kB pathway, upregulating CD86 statement, and immunological control by activating T cells. DPP-4 can advance inflammation in sufferers with type 2 diabetes, by regulating non- catalytic and catalytic metabolism. Thus, DPP4 inhibition has an impact on all these affected pathways in the immune system. DPP-4 inhibitors prevent the reduction of the incretins, which helps lower the blood glucose level. Interestingly, a study indicated that sufferers with diabetes and COVID-19 who are subscribed with DPP-4 inhibitors, express 64% less strict COVID-19. On the other hand, T cells play an important role in antiviral response, leading to cytokine storm. Based on studies, DPP-4/ CD26 have important function on T cells. It is predicted that DPP-4/ CD26 can interact with SARS-CoV-2 spike glycoproteins and this is a possible way for the virus to enter the cell and can infect the cell. The activation of T cells increases expression of CD26. The construction of TH1-type cytokines like interferon-gamma and CD26+ CD4+ T cells help differentiation of B cells into antibody-producing plasma cells. In addition, high expression of CD26 could have an influence on the migration of T cells. CD26+ T cells generate IL-2 by the interaction of CD26 and CD3 on T cells with plate-bound

monoclonal antibodies (mAbs). Thus, using DPP-4 inhibitors is a therapeutic way that can bind to DPP-4/CD26 and suppress all these pathways that could decrease risk of cytokine storm in COVID-19.

Conclusion: In conclusion, targeting DPP-4 receptors especially expressed on T-cells, have anti-inflammatory roles, helping improvement of sufferers with diabetes and COVID-19. Furthermore, it can be useful in decreasing the danger of severe COVID-19 in patients without diabetes. Based on this review, we suggest more investigation on CD26 immunotherapy, possibly as an appropriate treatment strategy for COVID-19.

Keywords: COVID-19; Dipeptidyl peptidase 4; CD26; DPP4 inhibitor; Diabetes

Impact of COVID-19 infection on maternal and neonatal outcomes: a review of 287 pregnancies (Review)

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Introduction: Pregnant women are vulnerable group in viral outbreaks especially in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. The aim of this review was to identify maternal and neonatal outcomes in available articles on pregnancies affected by COVID-19.

Methods: The articles that had assessed outcomes of pregnancy and perinatal of women with COVID-19 between Oct 2019 and Apr 30, 2020 without language limitation were considered. All kinds of studies such as case report, case series, retrospective cohort, case control were included. We searched databases, selected relevant studies and extracted data regarding maternal and neonatal outcomes from each article.

Results: Data of 287 pregnant women with COVID-19 of 6 countries were assessed from 28 articles between December 8, 2019 and April 6, 2020. Most pregnant women reported in their third trimester, 102 (35.5%) cases were symptomatic at the time of admission. Common onset symptoms, abnormal laboratory findings, and chest computed tomography pattern were fever (51.5%), lymphocytopenia (67.9%), and multiple ground-glass opacities (78.5%) respectively. 93% of all deliveries were done through cesarean section. No maternal mortality and 3 % ICU admission were reported. Vertical transmission was not reported but its possibility was suggested in three neonates. One neonatal death, one stillbirth, and one abortion were reported. All newborns were not breastfed.

Conclusion: This review showed fewer adverse maternal and neonatal outcomes in pregnant women with COVID-19 in comparison with previous coronavirus outbreak infection in pregnancy. Limited data are available regarding possibility of virus transmission in utero, during vaginal childbirth and breastfeeding. Effect of COVID-19 on first and second trimester and ongoing pregnancy outcomes in infected mothers is still questionable.

Keywords: SARS-CoV-2, pregnancy, pregnant women, maternal, neonate, infants, perinatal

Impact of interleukin 6 promoter polymorphisms -572 G > C on IL-6 levels and their impacts on the cancer development (Review)

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1.

Introduction: The results of relationships between IL-6 polymorphisms including G/C -572 and risk of different types of cancers including leukemia are debatable. Previous meta-analysis of the IL-6 gene offer indications for the existing understanding of the genetic contribution with some cancers.

Methods: We searched (for related studies), in PubMed, Scopus and google scholar published articles up recent year. The strengths of the relationships between IL-6 polymorphisms and numerous cancers risk were reviewed and discussed. We reviewed several case-control surveys involving cancer cases and healthy controls for the analysis.

Results: By means of of constrained qualified data, our study specifically attentive on SNPs of the IL-6 gene, -572 G/C. We perceived minimal significant involvement of -597 G/A polymorphisms with some cancers in the previously published articles on population. Other surveys accentuates the significance of -572G > C polymorphism in elevating IL-6 levels, thus displaying it's significant in leukemia.

Conclusion: Generally it could be indicate that -572G > C polymorphism detection may be one of the linking associations between IL-6 and leukemia,

Keywords: cancer, gene, polymorphism , leukemia

Impact of Single-Nucleotide Polymorphisms rs1143627 of IL-1β Genes on the Occurrence, Severity and Treatment Efectiveness of the Major Depressive Disorder (Research Paper)

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Introduction: Depressive disorder (MDD), also known as clinical/monopolar depression, affects more than 264 million people worldwide. This disease is considered to be the most common psychiatric/psychological disorder and is characterized by complex and very diverse physical, mental, and behavioral symptoms in individuals (especially for adults and the elderly). Despite the importance of the issue, the pathogenesis of depression is not fully understood. However, there is growing evidence that immunodeficiency and impaired immune regulation are associated with the pathophysiology of MDD. Inflammatory biomarkers of peripheral blood, including inflammatory cytokines, have been shown to increase in patients with major depression. The association of inflammation with major depressive disorder has been a valid hypothesis for more than a decade. In this study, we investigate the effect of rs1143627 single nucleotide polymorphism of interleukin-1 beta gene on the incidence, severity and effectiveness of major depressive disorder.

Methods: Find documents related to writing a review article in Google and Yahoo databases using the keywords MDD, Major Depressive Disorder, SNP, Single, Nucleotide Polymorphism, Interleukin, and interleukin-1 beta. The PubMed database was created and searched using medical subject headings. To select the documents used, the titles found by the search engine were first examined in terms of thematic relevance. After reviewing the aggression, the articles were evaluated in the next step in terms of the relationship between the abstract and the intended purpose. The selected cases were thoroughly studied and finalized.

Results: Inflammation, stress, and depression are closely linked. Evidence suggests that interleukin-mediated communication pathways between the immune system and the brain are involved in the pathogenesis of MDD. Of the many interleukins, IL-1β is one of the most studied in relation to MDD. In clinical and animal studies, the essential role of IL-1β in MDD and the performance of antidepressants have been reported. Interleukin-1 beta (IL-1β), a member of the interleukin-1 family, is a potent proinflammatory cytokine and plays an important role in several inflammatory and autoimmune diseases. IL-1β is mainly produced by blood monocytes and tissue macrophages (Charles A Dinarello, 1988). In humans, IL-1β is located on chromosome 2q14 and is expressed by several genetic polymorphisms in its regulatory region. Single nucleotide polymorphism (SNP) rs1799964 is located in the promoter region. In a 2012 study, its T / C and C / C genotypes were associated with decreased serum TNF-α levels. This study also reported a higher expression of the T allele gene compared to the C allele. Another study showed that the risk of depression was reduced in cases with the T / C-C / T genotype from rs1799964 - rs1143627, with rs1143627 in the TATA box motif in the promoter area. For the first time, a study in 2020 examined the relationship

between rs1143627 or rs17561 and MDD, in which the combined G / G - C / C genotype of rs1800629 - rs1143627 was identified to reduce the risk of depression. Evidence suggests that mental disorders, including major depressive disorder (MDD), bipolar disorder (BD), schizophrenia, and Alzheimer's disease (AD), can be thought of as inflammatory neurological disorders. An increased inflammatory response to stress or oxidative stress may cause microglia and lead to a significant increase in IL-1β levels. SNP genes encoding pro-inflammatory cytokines may affect the risk and treatment of depression.

Conclusion: Cognitive impairment has long challenged patients with major depressive disorder (MDD), and interleukins and inflammation have recently been shown to play a role in cognitive function. However, limited studies have evaluated their association with cognitive impairment in MDD. Examining the effect of studied SNPs on the effectiveness of antidepressant therapy suggests that there is a link between the presence of SNPs and the effectiveness of antidepressant therapy, in the hope that one-day immunosuppressive therapy will replace existing antidepressant or psychiatric medications.

Keywords: MDD, Major Depressive Disorder, SNP, Single Nucleotide Polymorphism, Interleukin

Importance of new synthesized cellulose nanocrystals from Ferula gummosa via hydrochloric acid and their biomedical application (Research Paper)

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Introduction: As environmental awareness grows, demand for renewable and natural materials is increasing. Cellulose is the most important natural biopolymer available on Earth. cellulose nanocrystals (CNCs) are promising nanomaterials with various applications in biomedicine.

Methods: In the present study, CNCs were extracted from ferula gommusa through hydrochloric acid (6 M, 1 h,45 °C). The plant of ferula gummosa has the potential to prevent the complications of diabetes by reducing the oxidative stress in the liver and kidneys. The prepared CNCs were characterized by x-ray diffraction (XRD), fourier transform infrared spectroscopy (FTIR) and field emission scanning electron microscopy (FESEM).

Results: The FESEM analysis of CNCs shows a semi-spherical shape. The result of XRD shows increase in crystallinity index and also decrease in crystalline size subsequent to the acid treatment. The FTIR confirms that the maximum amount of non-cellulosic materials is removed from roots of ferula gommusa after chemical process. These nanocrystals can be radiolabeled with fluorophores and some radiolabels in order to use them in medical imaging. The results of labeling showed that the most accumulation of CNCs have occurred in the kidneys and then liver which was in accordance with the requirements of this paper. After this, nanoparticles conjugated with ferula gummosa plant compounds in order to affect on kidneys and liver. The results of the ultraviolet absorption spectrum confirm the formation of the complex.

Conclusion: Functional modification of nanocellulose will determine the potential biomedical application for nanocellulose. So, the prepared CNCs from this medicinal plants can be use as antidiabetic agents or a vector in targeted drug delivery for well-being of diabetes.

Keywords: Cellulose nanocrystals; diabetes; radiolabel; ferula gummosa.

Improved BALB/c mice granulosa cell functions using purified alginate scaffold (Research Paper)

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Introduction: Alginate, a non-toxic polysaccharide isolated from brown algae, is a widely used 3-dimensional (3D) porous scaffold for the granulosa cell and follicle encapsulation. However, impurities in commercial alginate can lead to alginate biocompatibility reduction. The aim of this study was to evaluate in vitro behavior of the granulosa cells seeded on the purified alginate in varying concentrations compared with matched non-purified ones.

Methods: We produced a purified alginate using a simple and efficient method. Then, the granulosa cells from mice were isolated and seeded in various concentrations of (0.5%, 1% weight/volume) purified and non-purified alginate. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay was used on the 3rd, 5th and the 8th days of culture as an index of cell viability and proliferation. Furthermore, the secreted estradiol, progesterone and alkaline phosphatase enzyme (ALP) were measured in the granulosa cells culture media using radioimmunoassay kits.

Results: The data from the current study showed that alginate purification improved the viability and proliferation of granulosa cells. In comparison with the non-purified ones, there was a significant increase in survival and proliferation rates after 8 days of seeding in the purified alginate. Our study also showed that, alginate concentration had an effect on the murine granulosa cell proliferation and function. After the 8th day, the viability of the granulosa cells, estradiol and progesterone production in the 0.5% purified alginate gel was higher than those cultured in 1% alginate.

Conclusion: The results confirmed the impact of the alginate hydrogel properties on proliferative rate and function of granulosa cells in a 3D culture system.

Keywords: Alginate, Granulosa cell, Purification, Scaffold

Improvement of diabetic wound healing by topical application of acidified nitrite in type 2 diabetic rats (Research Paper)

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Introduction: Impaired nitric oxide (NO) production in the skin is a major contributor to the delayed wound healing in type 2 diabetes (T2D). The present study was designed to determine effects of acidified nitrite on wound closure as well as inflammatory and antioxidants markers in wound tissue of rats with T2D.

Methods: Control and diabetic Wistar rats were divided into four groups: Untreated control (C), acidified nitrite-treated control (CN), untreated diabetes (D), and acidified nitrite-treated diabetes (DN). T2D was induced using a high-fat diet followed by a low-dose of streptozotocin. A full-thickness excisional skin wound was made 28 days after the induction of diabetes on the back of rats. Acidified nitrite (20 mg) was applied once daily from day 3 to day 28 after wounding and wounds were photographed to evaluate CT50% (time taken for 50% closure of a wound), and wound closure percentage. Rats were sacrificed on days 3, 7, 14, 21, and 28 after wounding and wound tissue levels of nitrite + nitrate (NOx), tumor necrosis factor alpha (TNF-α), inducible nitric oxide synthase (iNOS), prostaglandin E2 (PGE2), total antioxidant capacity (TAC), and reduced glutathione (GSH) as well as activities of superoxide dismutase (SOD) and catalase were measured.

Results: Type 2 diabetic rats had delayed wound healing as demonstrated by ~2–fold higher CT50% and lower wound closure percentage compared to the controls. Compared with untreated diabetic rats, CT50% was significantly lower in acidified nitrite-treated diabetic rats (5.1 vs. 8.0 days, $p<0.001$). At days 3 and 7 after wounding, diabetic rats had lower levels of TNF-α, iNOS, and PGE2 within the wound tissue, whereas at day 14 after wounding, the parameters peaked in diabetic but not the control rats. These data indicate a delay in the inflammatory response at days 3 and 7 after wounding and persistence of the inflammatory response at day 14 after wounding in the diabetic rats, which is partially restored to control levels following topical application of acidified nitrite. A lower levels of antioxidant markers in diabetic wound, as observed in most time points. Levels of total antioxidant capacity (TAC) and reduced glutathione (GSH) as well as catalase activity (but not

SOD activity) were lower in type 2 diabetic rats at day 7 after wounding. Acidified nitrite increased SOD activity, decreased GSH level and had no effect on catalase activity and TAC levels in treated diabetic rats at day 7 after wounding.

Conclusion: Acidified nitrite accelerated wound healing in rats with T2D by restoring delayed inflammatory response and augmentation of antioxidant defense and may be a simple and non–expensive therapy to improve impaired wound healing in T2D.

Keywords: Acidified nitrite; Antioxidants, Diabetic wound; Inflammation; Nitric oxide; Type 2 diabetes.

In silico analysis of hsa-miR-181a-5p target genes and rs9266 relation with acute myeloid -leukemia (Research Paper)

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Introduction: Each year, nearly 60,000 people are diagnosed with leukemia. The development risk of Acute Myeloid Leukemia (AML) is considered to be increased by age. Leukemia is being listed as a genetic disease; genes are reviewed as one of the causes of this disease. As people could inherit genetic factors, based on the researches, miRNAs (small non-coding RNAs) and SNPs (single nucleotide polymorphisms) might develop the chance of being infected by Leukemia. This study has been done in order to diagnose a potential biomarker for early detection of AML. According to bioinformatics analysis, hsa-mir-181a-5p, which is located on chromosome 9, was selected for this survey.

Methods: As this research was done based on bioinformatics analysis miRbase, miRTarbase, miRWalk, TargetScan, DIANA TOOLS, DAVID, miRdSNP, miRNASNP, miRSNPdb, GeneMANIA databases and Cytoscape 3.8.0 software were needed to get proper data of micoRNA basis, validated and predicted target genes, gene's expressions, signaling pathways, SNP and genes' interaction networks.

Results: According to the hsa-mir-181a-5p targets PDPK1, AKT3, HRAS, SOS1, MAPK1, MAP2K1, PTEN, PIK3CB, PIK3R3 genes are considered as the most frequent genes of FoxO, PI3K-AKT and Focal adhesion signaling pathways of Acute Myeloid Leukemia which their similar pattern is clearly notable. Furthermore, in the bioinformatics analysis of this study, the occurrence of rs9266 in KRAS, one of the AML disease genes, showed to have vital role in AML disease process, but to understand the role of this SNP in AML a wide range of surveys are required.

Conclusion: According to PI3K-AKT signaling pathway, some genes, including MAP2K1, MAPK1, BCL2, CDKN1B, HRAS seem might lead to metastasis via causing cell proliferation, angiogenesis. Moreover, in Focal adhesion pathway, MAPK8 gene which activates via a cascade of genes, is able to trigger cell proliferation. Thus, inhibition of these genes by hsa-mir-181a-5p that lead to metastasis and proliferation, mentioned miRNA is considered to be tumor suppressive.

Keywords: Bioinformatics, miRNA, SNP, AML, Signaling pathway

In Silico Molecular Docking Studies of Phenolic Compounds in Cucumis melo L. Seeds as Potential Inhibitors of Myeloperoxidase (Research Paper)

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Introduction: Myeloperoxidase (MPO) as an inflammation and oxidative stress maker is one of the main heme peroxidase enzyme involved in the acute and chronic inflammatory diseases promotes oxidative stress and mainly expressed by activated neutrophils, monocytes and selected tissue macrophages. MPO and its downstream inflammatory pathways present potential targets for discovery and development of therapeutic drugs for cardiovascular diseases, inflammatory diseases, kidney and liver diseases, immune-mediated diseases and neurodegenerative diseases. Discovery and development of bioactive natural compounds that can efficiently inhibit MPO activity to subsequently decrease inflammatory events has been focus of the current research interest. Natural compounds that have been used traditionally as nutrition or medicine may also act as anti-inflammatory agents. Cucumis melo L. belongs to Cucurbitaceae family is one of most widely consumed vegetable with remarkable economic, nutritional and medicinal values. Phenolic compositions of functional bioactive components of melon seeds possess therapeutic effects such as antioxidant, anti-inflammatory, and analgesic properties. The aim of this study was to analyze the potential MPO inhibitory activity of natural compounds in Cucumis melo L by computational docking studies.

Methods: The initial structure for the molecular docking of MPO with phenolic compounds was obtained from RCSB PDB (https://rcsb.org). The x-ray crystallography structure of human MPO with the 5FIW PDB ID was downloaded. UCSF Chimera 1.11.2 was used for preparing the receptor for docking by removing its ligands, ions and water molecules. The chemical structures of the 10 natural compounds and triazolopyrimidine a chemical inhibitor of MPO as control were retrieved from PubChem compound database. The ligands structures were prepared by ChemBioDraw and MOL SDF format of them for generating the atomic coordinates were converted to PDBQT file using PyRx tool. The ligand binding site of MPO was predicted using 3DLigandSite server. The docking experiments were performed using AutoDock 4.2.6 for docking of the ligands to grids describing the MPO as a target. We used AutoGrid for pre-calculating these grids as well as AutoDock graphical user interface called AutoDockTools (ADT) for setting up, running and analyzing the docking experiments.

Results: As assessed from literature search, 10 phenolic compounds from Cucumis melo L. including gallic acid, procatechuic acid, chlorogenic acid, vanillic acid, rosmarinic acid, luteolin, apigenin, flavone, amentoflavone and hydroxytyrosol were selected for molecular docking studies. The principle interactions of these natural compounds and MPO were revealed by molecular docking. The principle amino acid residues associated with ligand binding were revealed by active site analysis. Docking studies against MPO revealed that all phenolic compounds form

H-bonds with MPO. Gallic acid interacted with MPO by forming two hydrogen bonds. All ligands were suitably docked on MPO macromolecule (−5.31 to −6.41kcal/mol) with promising score. The results have indicated that among these 10 natural compounds in Cucumis melo L., gallic acid showed higher binding affinity compared to others with the lowest binding energy (-6.41kcal/mol) and the favorable pose in active site of MPO and probably potential anti-inflammatory effect. Triazolopyrimidine showed -6.08kcal/mol binding energy. The docking site of these natural compounds and triazolopyrimidine were noteworthy similar.

Conclusion: Our findings demonstrate the potency of phenolic compounds of Cucumis melo L.seeds for discovery and development of new MPO inhibitors with less toxicity and more selectivity than chemical inhibitor and prove that dietary antioxidants like melon can be effective for treatment of a number of pathologies with compelling evidence in initiation and progression of inflammatory events. Since the binding energies of natural compounds of melon studied herein were comparable to chemical MPO inhibitor, these computational preliminary results need experimental confirmation in near future to generation of novel drugs for numerous inflammatory pathologies.

Keywords: Molecular docking, Myeloperoxidase, Cucumis melo L., Natural inhibitor, Inflammation

In silico prediction and analysis of influenza A (H5N1) Indonesian virus neuraminidase protein epitopes as a clue for diagnostic tests and effective vaccines development (Research Paper)

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Introduction: In the year of 2007, the avian influenza outbreak which occurred in Indonesia caused mortality of almost 85% from detected avian influenza cases. Comparing the mortality rate in Indonesia to other countries with avian influenza outbreak, WHO announced the Highly Pathogenic Influenza (HPIV) Indonesia virus has the highest pathogenicity. Mutations with either antigenic shift or antigenic drift can influence the pathogenicity of the influenza virus. Studies on neuraminidase (NA) have been carried out because the protein has important roles in the infection process of the avian influenza virus and pathogenicity of birds to humans. So, the prediction of epitopes in protein provides a suitable primary immunodiagnostic antigen for the detection of the influenza A virus H5N1.

Methods: In silico analysis was done to find potential T-cell and B-cell epitopes. At first the nucleotides and protein sequences of neuraminidase of influenza A virus (A/Indonesia/5/2005(H5N1) were taken from NCBI Genbank (Accession number: EU146623.1)and the open reading frame (ORF), a restriction site, expected molecular weight, and isoelectric point (pI) value were analyzed with Generunner and Prot Param softwares. The three-dimensional structure of the protein was predicted by the softwares available on the Expasysite. Amino acid sequence epitopes after NA gene expression for B lymphocytes and T lymphocytes by ABCpred and CTLpred respectively checked out and MHC class, I and II constructed for epitopes after NA gene expression was predicted in the IEDB database. The immunogenicity and stability indices of the amino the acid sequence was examined using Ellipro (an online tool that predicts the three-dimensional structures of protein using PDB format).

Results: As a result of the prediction of linear and discontinuous epitopes of the amino acid sequence of the protein neuraminidase and their antigenicity by the Ellipro database, the predicted epitope regions were fully visible on the three-dimensional molecular structure. Comparison of B-cell linear epitopes obtained from the first structure and discontinuous epitopes from the structures shows that

there are some antigenic regions of the molecule in both structures that have the potential to stimulate the humoral immune system and produce antibodies. A result of MHC class I and II prediction observed showed that NA epitopes stimulate both cellular and humoral immune systems.

Conclusion: These results showed that this protein is a good candidate for the production of diagnostic tests and effective vaccines.

Keywords: H5N1 Indonesia, neuraminidase (NA), vaccine, diagnostic test, In silico.

In vitro evaluation of silibinin effect on insulin like growth factor-1 (IGF-1) expression in human foreskin fibroblast (Research Paper)

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Introduction: Fibroblasts are fixed cells of connective tissue, but throughout life, they mamtain their growth and repair potency. Moreover, they are involved in production of growth factors which are effective on cells growth and differentiation. These cells are the most adaptable cells in connective tissue that pose significant capacity for differentiation to the other members of this cell group. Insulin-like growth factor-1 (IGF-1) is a hormone similar in molecular structure to insulin. It plays an important role in childhood growth and contimues to have anabolic effects in adults and in differentiation and growth of various cell limes. Silibinin is the most important and active component of silymarin, which is extracted from seeds of Silybum marianum, belongs to Asteraceae aster family, This compound has some anti-infammatory, anti-oxidant, and anti-proliferative properties.

Methods: In this study we evaluated the silibinin effect on viability and IGF-1 gene expression in human foreskin fibroblast (HFF). First, the cytotoxic effect of silibinin in 10, 20, 40 & 60 µM on HFF cells was evaluated using MTT assay, after 24 & 48 hours. Then, the expression of IGF-1 gene was evaluated after extraction of RNA from the HFF cells and by means of real time-PCR test Based on MTT assay results.

Results: silibinin had toxic effect on HFF cells in dose-dependent manner after 24 hours of incubation but in contrast. it was not significant after 48 hour Besides, after 24 hour of incubation, silibinin with a concentration of 20-60 µM significantly increased the IGF-1 gene expression in fibroblast cells in comparison with control group. Based on the results; probably silibinin in dose dependent manner siguificantly induces IGF-1 gene expression after 24 hour incubation with HFF cells However, in cytotoxicity assay, concentration of 60 µM caused the highest rate of cell death after 24 hours.

Conclusion: So, for introduction this compound as a stimulant of fibroblasts proliferation, more exteusive studies are needed.

Keywords: Silibinin,Fibroblast,IGF-1.

In-silico analysis of hsa-mir-17-5p in hepatocellular carcinoma (Research Paper)

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Introduction: Hepatocellular carcinoma (HCC) is not only the most frequent liver primary cancer but also a leading cause of cancer related to death in worldwide. There are many genetic factors which may be able to increase the risk of cancer infection. According to the researches, miRNAs (small non-coding RNAs) and SNPs (single nucleotide polymorphisms) might develop the progression of hepatocellular carcinoma. A large-scale of studies lead us to hsa-mir-17-5p of chromosome 13 for bioinformatics analysis of hepatocellular carcinoma.

Methods: To perform a wide range of bioinformatics analysis miRBase, miRTarbase, miRWalk, TargetScan, DIANA TOOLS, DAVID, miRdSNP, miRSNPdb, miRNASNP, GeneMANIA databases, R programming language and GraphPad Prism 8.0 were needed to get required data about micoRNA basis, validated and predicted target genes, signaling pathways, SNP and genes' interaction networks, genes' expressions and genes' expression analysis by Heatmap.

Results: The bioinformatics analysis has been demonstrated that, INSR, MAPK1, AKT3, PIK3CA, PIK3R1, PIK3R2, PIK3R3 as the most frequent genes of hsa-mir-17-5p in Ras, JAK-STAT, Rap1 signaling pathways could have impact on hepatocellular carcinoma progression. In addition, based on a number of analysis, rs3739008 of NPAS2, a target gene, has been detected as a biomarker which might be involved in hepatocellular carcinoma process. Furthermore, via heatmap analysis, the expression of PIK3R2 gene devoted the largest difference among solid tissue normal and primary solid tumor in hepatocellular carcinoma, that might develop a promising diagnosis and treatment for hepatocellular carcinoma.

Conclusion: Based on the studies, it has been revealed that likely hsa-mir-17-5p via inhabitation of SOS1, Akt3, PIK3R3, PIK3R2, PIK3R1, PIK3CA genes by Ras, Rap1 and JAK-STAT signaling pathways which control stem cell proliferation, differentiation, migration and motility suppresses hepatocellular carcinoma. NPAS2 gene is one of the vital genes of hepatocellular carcinoma, that occurrence of rs3739008 in this gene, revealed to have impact on this carcinoma via effecting the target genes function through cancer process.

Keywords: Bioinformatics, miRNA, SNP, Hepatocellular carcinoma, Signaling pathway

Increasing fertility IUI procedure in ischemia/Reperfusion treated with hydroalcoholic clove extract powder in adult female mice (Research Paper)

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Introduction: Considering the significance of reproduction in animal survival , finding a way to eliminate of sterility among women in Torsion or Ovarian Torsion ,of which appropriate untreatment by interruoting perfusion to ovarian will cause to destroy it.Using herbs has been the basis of traditional medicine , and nowadays these plants are the structural basis of chemical drugs, too. Carnation has always been attracted among various herbs and spices,because of its abtioxidant properly and likely it can be a suitable choice to improve or treat sterility induced by ovarian torsion.On the other hand,numerous clinical and experimental treatments for sterility are in progress,one of which is IUI. This method is cost-effective and less invasive than IVF .

Methods: In the present study ,protective effact of incubated hydroalcoholic extract of carnation on torsioned ovarian in rats and also on sterility treatment induced by Ischemia/Reperfusion following IUI method, was studid. For this purpose,20 rats were randomlyd divided into 4 groups. After implementing IUI ,the number of pregnant rats by method was counted:Sham group as control group,group2 :rats under torsion which did not receive treatment with hydroalcoholic carnation extract,group 3:rats which were torshioed and treated by 30 mg or carnation,group 4: rats which were torshioned and treated by 60 mg of carnation extract.

Results: The results indicated that use of this plant is effective on increasing ovarian follcles of female rats and the number of offspring thtough follicle.

Conclusion: It seems that incubated hydroalcoholic oxtract of carnation plays a role in treating sterility, hence, it is suggested for supplementary studies of animal and human.

Keywords: Ovarian Torsion, Rats, Ischemia/Reperfusion, IUI

Infertility Problems in Young Women with Breast Cancer Undergoing Chemotherapy: A Systematic Review and Meta-analysis (Review)

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Introduction: The purpose of the present study was to systematically review infertility problems on patients with breast cancer, conduct a meta-analysis, if possible, and to emphasize the main points of proper treatment, including some available choices to keep fertility.

Methods: 108 titles and abstracts were found from databases of MEDLINE, EMBASE, Scopus, Cochrane, and web of science data. Nine articles have been chosen for systematic review after duplicate elimination and selection of eligible ones were included with criteria such as young female breast cancer with concerns related to fertility, ovarian failure or fertility-related symptoms, and upper 50 years' age limitation.

Results: Nine studies were included in this systematic review, from which seven studies (2014 - 2018, n = 1697 women), by choosing newer studies on single populations went under meta-analyzed. It was revealed that the prevalence of infertility in women with breast cancer with a range of 48.5% (95% CI: minimum of 25.5% and maximum of72.2%) was significant. This would be an important issue for young breast cancer survivors, whether going for fertility preservation or not.

Conclusion: Young breast cancer survivors should be awarded the issues related to fertility and be prepared to discuss options for fertility preservation. Due to the limited studies, the results should be going under further validations by vaster heterogeneity and in cohort studies with short-term parameters, biomarkers related to ovarian function evaluating the infertility problems; and there would be a demand for further studies on better therapies shortened the consequences on the fertility.

Keywords: Breast Cancer, Drug Therapy, Reproductive Age, Adjuvant Chemotherapy

Influence of helicobacter pylori infection and gastritis on ghrelin levels and its receptors expression. (Research Paper)

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Introduction: Recently it has been shown that the ghrelin axis plays an important role in preventing the progression of carcinogenesis processes. It seems that alterations in this axis can play an undeniable role in the occurrence and development of pathological conditions. Moreover, Changes in the components of this axis have been reported in various cancers, such as gastric cancer. As far as we know, Helicobacter pylori (H. pylori) infection and its associated gastritis are the most important risk factors for non-cardia gastric cancer. So, identifying the molecular mechanism by which this infection progresses to cancer is crucial. Until today, some studies have shown that ghrelin levels changes in H. pylori infected patients. However, no study has examined the changes in Growth hormone secretagogue receptor 1a (GHSR1a) and GHSR1b in this patients.

Methods: In this study we enrolled 68 adult people, Individuals were classified into three groups based on two factors: H. pylori infection and Gastritis. Diagnosis of H. pylori infection was determined by RUT test and microscopic observation, also gastritis status was classified according to the updated Sydney System by pathologists. Total ghrelin levels was measured by ELISA Sandwich method using a commercially human ghrelin ELISA kit. The expression level of GHSR1a and GHSR1b mRNA was evaluated by using a real-time quantitative RT-PCR method.

Results: Out of the 68 subjects, 31, 28 and 9 subjects were H. pylori positive with gastritis, H. pylori negative with gastritis and H. pylori negative without gastritis respectively. Serum ghrelin levels was significantly lower in H. pylori positive with gastritis patients compared with both H. pylori negative with and without gastritis, (P value = 0.008, 0.01). GHSR1a mRNA expression was not different between groups, while GHSR1b expression was significantly higher in patients with H.pylori infection and gastritis.

Conclusion: Our results revealed that H. pylori infection and gastritis can affect the ghrelin axis, thereby this axis can be a new useful insight and potential clinical consequence in the gastric disorders.

Keywords: Helicobacter pylori, Ghrelin, Gastritis, Body Mass Index,

Inhibition of alpha-synuclein by plant extract (Research Paper)

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Introduction: Parkinson is a progressive neurodegenerative disease caused by environmental and genetic factors which is known by motor symptoms including bradykinesia, resting tremor and movement rigidity. loss of dopamine secretion, and aggregation of α-synuclein are main causes of Parkinson disease symptoms. One of the genetic factors involved in the disease is the PARK1 gene, which is located on chromosome 4, and codes synuclein family protein. The misfolding and aggregation of the synuclein protein (α -syn), which results in the formation of amyloid fibrils, is involved in the pathogenesis of Parkinson's disease and other synucleinopathies. in addition, α-Synuclein may be the main component of the Lewy body in Parkinson's disease. Alpha-Synuclein is a small protein with 41 amino acids, which is free of friction in normal conditions. The protein is divided into three parts in terms of building characteristics. The middle part is hydrophobic and contains a highly repeatable sequence of glycine, proline, valine and alanine amines that plays a major role in the initiation of the pudding folding process. small molecules as a drug can be taken orally and are better at reaching different sites in the body. Our aim is to engineering herbal based ligand to inhibit a-syn aggregation.

Methods: Protein structure provided from Protein Data Bank with PDB access code of 4BXL. molecular docking methods explore the ligand conformations adopted within the binding sites of α-Synuclein as targets.in this study, autodock Vina under PyRX software as the virtual screening software was used and analysis of the absorption, distribution, metabolism and excretion properties (ADME) of virtual screening hits were studied by using FAF Drugs 4 web server. ligands were engineered using hyperchem software based on the structure of top hits retrieved from virtual screening process. New rationally designed ligands were then analyzed regarding ADME and toxicity to reach optimal scores.

Results: according to the information we were able to get the h-band from -6 to -9 and it is hypothesized that this drug can be used.

Conclusion: -

Keywords: alpha-synuclein -parkinson- neurodegenerative disease -Lewy body

Inhibitory effect of chitosan nanoparticles on the growth of Pseudomonas aeruginosa (Research Paper)

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Introduction: Pseudomonas aeruginosa is one of the most important pathogenic and opportunistic bacteria that has antibiotic resistance to some of antibiotic such as Penicillin. This bacterium is the third most common infection cause in most hospitals so considering the importance of pathogenicity, finding a way to inhibit its growth is very important. One of the best and least harmful ways to prevent the growth of this bacterium is to use nanoparticles and chitosan nanoparticles with their biodegradability can be a great choice. The aim of this study is to find an effective way with the least side effects to inhibit and prevent the growth of this bacteria.

Methods: In the first, the antibiotic effect of chitosan nanoparticles on Pseudomonas aeruginosa was investigated by MIC (Minimum Inhibitory Concentration) and MBC (Minimum Bactericidal Concentration). Different concentrations 0.5, 1, 2 and 4 of chitosan nanoparticles were investigated, also disk diffusion and well method in Muller Hinton broth and agar were performed.

Results: As a result, Different concentrations of nanoparticles had different effects on bacteria, the inhibitory effect also increased with increasing the concentration of nanoparticles, the inhibitory effect also increased, so that the concentration of 0.5 had the least inhibitory effect and the concentration of 4 had the most inhibitory effect on the growth of bacteria.

Conclusion: According to the results of the study, the use of chitosan nanoparticles can be an excellent option to prevent the growth of this pathogenic bacterium. Also, the use of these nanoparticles can be a good alternative to antibiotics and does not have the side effects of using antibiotics, and the use of these nanoparticles can be considered a significant development in the pharmaceutical industry.

Keywords: Pseudomonas aeruginosa, Inhibitory effect, Chitosan nanoparticles, Infection

Interaction between the dietary indices (DQI, DPI, HEI) and PPAR-γ gene variants on cardiovascular risk factors in a patient with type 2 diabetes mellitus (Research Paper)

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Introduction: Cardiovascular disease is one of the major complications in patients with type 2 diabetes mellitus (T2DM). Dietary indices including DQI, DPI, and HEI and genetic variants of PPAR-γ Pro12Ala polymorphism could also affect lipid profile concentrations, inflammatory markers, ghrelin, and leptin hormones. Therefore, we decided to study the interaction between PPAR-γ Pro12Ala polymorphism and dietary indices (DQI, DPI, HEI) on cardiovascular disease risk factors in patients with T2DM

Methods: This cross-sectional study was conducted on 393 diabetic patients. PPAR-γ Pro12Ala polymorphism was genotyped by polymerase chain reaction-restriction length polymorphism (PCR-RFLP). Biochemical markers including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), superoxide dismutase (SOD), C-reactive protein (CRP), total antioxidant capacity (TAC), pentraxin-3 (PTX3), isoprostane F2 α (PGF2α) were measured by standard protocol. FFQ was used for estimating food intakes and dietary indices (DQI, DPI, HEI) were calculated

Results: There was no significant relationship between PPAR-γ Pro12Ala polymorphism and cardiovascular disease risk factors. The rs1801282-DQI interactions were significant on WC in both crude and adjusted models (P Interaction = 0.02 and P Interaction = 0.01). Thus, C-allele carriers in the higher tertile of DQI had higher WC measurements compared to GG homozygous. Further, an interaction was observed between PPAR rs1801282 polymorphism and DQI on serum IL-18 level (P interaction= 0.03). Besides, a significant rs1801282-DPI interaction was shown on HDL concentration (P Interaction= 0.04) in the adjusted model, carriers of the G allele who were in the highest tertile of DPI, had lower HDL. Moreover, there were significant rs1801282-HEI interactions on ghrelin (P Interaction = 0.04) in the crude model and leptin plasma levels (P Interaction= 0.02) in the adjusted model. Individuals with (CC, CG) genotypes in the higher tertile of HEI, had lower leptin and ghrelin concentration.

Conclusion: Higher dietary indices (DQI, DPI, HEI) may affect the relationship between PPAR-γ Pro12Ala polymorphism and waist circumference and ghrelin, leptin, HDL-c, IL-18 concentration in patients with T2DM.

Keywords: PPAR-γ; Gene-environment interaction; Personalized diet; Cardio-metabolic disease

Interactions Between Caveolin-1 (rs3807992) Polymorphism and Major Dietary Patterns on Cardio-metabolic Risk Factors Among Obese and Overweight Women (Research Paper)

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Introduction: Caveolin is a cholesterol-dependent essential component located in caveolae. Several studies have been shown CAV-1 SNP related to cardio-metabolic parameters in animal models, however there is few studies in humans. Importantly, there is no study has investigated the interaction between CAV-1 rs3807992 gene and dietary pattern on CVDs risk factors in Iranian population.

Methods: The current cross-sectional study was conducted on 404 overweight and obese females with mean age of 36 years. Dietary intake obtained from FFQ with 147 items. The CAV-1 genotype was measured by the PCR-RFLP method. The anthropometric measurements, serum lipid profile and inflammatory markers were measured.

Results: : There was a significant interaction between CAV-1 rs3807992 and healthy dietary pattern on HDL (P interaction=0.03), TC/HDL (P interaction=0.03) and hs-CRP (P interaction=0.04); in A-allele carriers, higher adherence to the healthy dietary pattern was related to higher level of HDL and lower TC/HDL and hs-CRP. As well as, the significant interactions were observed between CAV-1 rs3807992 and unhealthy dietary pattern in relation to TG (P interaction = 0.001), AST (P interaction = 0.01) and MCP-1(P interaction = 0.01); A-allele carriers were more adherence to the unhealthy dietary pattern to lower levels of TG, AST and MCP-1

Conclusion: : There was a significant interaction between CAV-1 rs3807992 and healthy dietary pattern on HDL (P interaction=0.03), TC/HDL (P interaction=0.03) and hs-CRP (P interaction=0.04); in A-allele carriers, higher adherence to the healthy dietary pattern was related to higher level of HDL and lower TC/HDL and hs-CRP. As well as, the significant interactions were observed between CAV-1 rs3807992 and unhealthy dietary pattern in relation to TG (P interaction = 0.001), AST (P interaction = 0.01) and MCP-1(P interaction = 0.01); A-allele carriers were more adherence to the unhealthy dietary pattern to lower levels of TG, AST and MCP-1

Keywords: Diet; Gene-environment interaction; Caveolin 1; Cardio-metabolic; Personalized medicine

Introduction of Natural Killer Cells and their role in inflammation (Review)

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Introduction: Natural Killer Cells (NK Cells) are members of the innate immunity system, which are responsible for protecting their host against tumors and pathogen-infected cells, as well as activating macrophages and maintaining immune homeostasis. The main function of NK Cells is to release perforin, followed by granzymes using effector molecules such as TNF, Fas ligand, and so on which eventually leads to the killing of infected cells. In fact, it can be said that one of the main functions of NK cells to protect the host is to secrete IFN-γ. One way to accurately identify NK Cells is through their surface proteins. For example, in the human immune system, NK Cells are identified based on the expression of CD56, but most of them express CD16. NK cells are said to have cytolytic properties, and this feature is obtained by a single evolution in the thymus without the need for re-evolution. NK Cells originate from hematopoietic stem cells in the bone marrow and are mostly lymphoid progenitor cells. They consist about 5-20% of the volume of blood lymphocytes and are present in very small amounts in tissues and lymphatic organs. NK Cells are equipped with an advanced repertoire to identify their targets. In general, three types of receptors regulate the response of NK Cells: cytokine receptors, activating receptors, and inhibitory receptors. Activation of NK Cells) There are several mechanisms for activating NK cells, but in this article, we will mention only two mechanisms. In one mechanism, NK cells can be activated using cytokines or by interacting with a pathogen. In this case, cells stimulated by pathogens through Toll-like receptors, including epithelial cells, etc., secrete cytokines that directly affect NK cells and stimulate cytokine and chemokine production. Another mechanism for activating NK cells is based on the ability of NK cells to express the activator of CD-16 in killing target cells by IGG-coated by a process called antibody-dependent cytotoxicity. NK cells are generally divided into four main subgroups: 1) The CD56 bright NK Cells represent the CD62L 2) The CD56 dim NK Cells represent the PLZF 3) The CD56 bright NK Cells with low or no expression of PLZF 4) The CD56 bright NK Cells tissue reside In response to the involvement of NK cells with target cells, these cells can produce a wide range of cytokines and interleukins such as IFN-γ and TNF, IL-5, IL-10, IL-13, GM-CSF growth factor and secrete chemokines such as CCL3, CCL4, CCL5 and, CCL8. Approximately 10% of the NK Cells in the peripheral blood express a large amount of CD56 and are thus known as CD56 bright cells. NK Cells in inflammation) Severe inflammation is associated with a wide range of diseases and in very severe forms, death. For example, in human, congenital defects in lymphocyte cell cytotoxicity cause life-threatening hyper-inflammatory syndrome, which typically occurs in infancy. Another evidence linking NK Cells to inflammation comes from asthma studies. In mild to moderate asthma, among the molecular mediators, lipoxin A4 increases eosinophil apoptosis, which is characterized by inflammation of the airways. But the same inflammation in severe asthma leads to a relative

increase in CD56dim NK Cells, which is inversely related to lung function. It is thought that the suppressive action of corticosteroids may also lead to pneumonia.

Methods: In the first study, the role of NK cells in allergic inflammation was investigated. The second study was performed to investigate the effect of NK Cells on the pathology of airway diseases.

Results: In the first study, it was found that in inflammations, especially peritoneal inflammation, defects in NK cells could reduce eosinophilia and produce IL-15. In the second study, NK cells were found to be able to increase allergic airway inflammation during allergies and inflammation. It was also found that if stimulated by IFN-γ, the damage caused by allergic inflammation is reduced.

Conclusion: Our understanding of NK Cells, their structure and function has made great strides since the discovery of these cells. Various studies have confirmed the role of NK Cells in inflammation. Of course, more studies are needed to fully understand the role of NK Cells. These studies may shed light on new facts that could lead to the discovery of newer treatment opportunities.

Keywords: NK Cells, Inflammation, Cytolytic, Innate immunity

Investigate the therapeutic effects of bone marrow-derived mesenchymal stem cells transplantation on Asherman's syndrome (Review)

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Introduction: Asherman's syndrome (AS) can occur following uterine curettage, Instrumentation, or infections in the pregnant or recently pregnant uterine cavity. AS is a rare condition, although it has been reported in 13% of infertile patients and 7% of women with secondary amenorrhea. Women with AS have amenorrhea or hypomenorrhea, cyclical pelvic pain, endometriosis, infertility, and recurrent spontaneous abortions. Some reports suggest that bone marrow stem cells (BMSCs) may serve as a source of stem cells for endometrial regeneration in AS. These cells are one type of adult stem cells with the characteristics of self-renewal, multipotential differentiation, autotransplantation without immune rejection. This review aims to determine the therapeutic effects of BMSCs on AS.

Methods: Articles from 2010 to 2020 were collected from PubMed, google scholar, medlib, irandoc, ISC, SID, and Cochrane databases. Totally 638 articles were found. 620 articles were excluded by reading the title. 6 articles were excluded after reading the title and 1 article was excluded after reading the full text. Finally, 11 articles were selected. All selected articles were in English.

Results: 4 studies show that BMDSCs promote endometrial regeneration and restore fertility in patients with AS. 2 of these articles were clinical trials. In one of these articles, the method was hormonal replacement therapy (HRT) and then BMDSC injected through the femoral artery and menstruation restarted after 6 months and 2 successful pregnancies were achieved. In another study, BMDSCs injected intrauterine tow times and after the second time, all 5 patients became pregnant. 5 articles performed on mice showed that treatment with BMDSCs improves fertility after uterine injury and plays a functional role in the regeneration of endometrium. The results of an article performed on mice aren't in agreement with the current articles and provide no evidence that BMSCs can transdifferentiate into the endometrial epithelium. 1article shows that CD133+ or prominin-1 which is a surface antigen that defines a broad population of somatic stem cells can be useful in the treatment of AS.

Conclusion: Stem cell therapy is a promising novel approach for resistant cases of AS. Bone marrow is a well-known store of mesenchymal stem cells. BMSCs can be injected in both local and systemic transplantation and result in endometrial regeneration by increasing epithelial thickness and vascular endothelial growth factor expression, and decreasing the percentage of collagen deposition. We suggest that intrauterine injection is better because the number of cells that inject into the vein is more than local injection. Injected cells into the vein travel a farther

distance to reach the target area and these cells are more likely to die due to exposure to blood toxic factors.

Keywords: Bone marrow-derived stem cell, Mesenchymal stem cells, Asherman syndrome, Intrauterine adhesion

Investigating association of Cytokine genes with polycystic ovary syndrome (PCOS) risk: A systematic review (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is a common and complex gynecological endocrine disorder that affects approximately 6% to 10% of women of their reproductive age. The exact etiological mechanism of PCOS is still under debate; however, there is evidence that genetic factors play a vital role. Cytokine genes polymorphisms may play an important role in the etiology of PCOS.

Methods: This review was performed within articles published at PubMed, Scopus, and Web of Science from 2015 to 2020. The keywords were Cytokine genes; Inflammation; Polycystic ovary syndrome. By searching this database, 68 articles were found, 24 of them were not related to investigating, and 19 of them by reading abstract were removed. All articles chosen from English papers.

Results: As a common multifunctional cytokine, IL-6 has been proven to influence the processes of fertilization, implantation, and ovulation, which are also affected in women with PCOS. Some genetic studies have been performed to investigate the associations between IL−6 rs1800795 polymorphism and PCOS risk; however, the results were inconclusive. A single study lacks sufficient statistical power to confirm the relationship between rs1800795 and the risk of PCOS because of the small sample size. Some studies focused on the associations between TNF-α and Interleukin gene polymorphisms and polycystic ovary syndrome (PCOS) risk, but the results remain controversial. A study showed that an increase in both low-grade chronic inflammation and insulin resistance in PCOS patients is associated with increased central fat excess rather than PCOS status. It remains to be established whether the proinflammatory state in PCOS is primarily a result of genetic variation or simply inflamed adipose tissue, because there is an increased prevalence of abdominal adiposity in PCOS across all weight classes. In fact, no differences were reported in levels of TNF-alpha, IL-6, and markers of inflammation between obese women with PCOS and obese controls. Furthermore, it has been suggested that obesity-associated genes, environmental factors, and dietary habits are also responsible for the increasing prevalence of PCOS worldwide.

Conclusion: Future multi-ethnicity studies of homogeneous populations of PCOS patients with larger sample sizes and well-matched controls are needed. future genetic studies should include larger sample sizes and investigation of SNPs within these genes to uncover the causal SNP variant associated with PCOS in different ancestries. Also, SNPs in inflammatory genes seem unrelated to PCOS, and require additional investigation, especially in the context of obesity and PCOS.

Keywords: Cytokine genes; Inflammation; Polycystic ovary syndrome.

Investigating association of TOX3 gene expression in cancer patients (Review)

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Introduction: During the malignant process, cancer cells acquire multiple alterations genetic that override the normal mechanisms controlling cellular proliferation. In brief, cancer is a disease of genetic abnormalities caused by hereditary and environmental factors. The protein encoded by TOX3 gene contains an HMG-box, indicating that it may be involved in bending and unwinding of DNA and alteration of chromatin structure. A minor allele of this gene has been implicated in an elevated risk of breast cancer, stomach, esophagus, SCC (Squamous cell carcinoma) and 13 other tissues; so the aim of this study is investigating of TOX3 gene expression in cancer patients.

Methods: This review was performed within articles published at PubMed, Google scholar and SID from 2016 to 2020. The keywords were TOX3 gene, expression, cancer and breast cancer. By searching this database, 47 articles were found, 19 of them were not related with investigating and 12 of them by reading abstract were removed. All articles chosen from English and Persian articles

Results: Finally 16 articles were included in the study. Some studies showed that breast cancer-associated SNPs reduce the expression of the TOX3 gene. Although there are articles that determine; high expression of this protein plays an important role in breast cancer progression. Together, these results suggest two different roles for TOX3, one in the initiation of breast cancer that potentially related to expression of TOX3 in mammary epithelial cell and another role for this nuclear protein in the progression of cancer. In addition, these results can show association of TOX3 expression and breast cancer metastasis to the bone. In another studies a significant decrease in the expression of this gene in SCC (Squamous cell carcinoma) was observed also a number of articles have shown the role of TOX3 in gastric cancer.

Conclusion: It seems that TOX3 gene expression has reduced in most studies on breast, gastric, and even esophageal cancer. But there are few studies that give us a conclusive result, And it is suggested that more research done to elucidate the exact mechanism of action of the gene as a tumor suppressor in any of these cancers and the expression pattern or biological role of TOX3 in these cancers and also need to perform in more human sample and different areas of worlds.

Keywords: TOX3 gene, Expression, Cancer, Breast cancer

Investigating change of AkT gene expression in the T98G Glioblastoma cell line under treatment with thiosemicarbazones complexes (Cu) (Research Paper)

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Introduction: A brain tumor is an abnormal mass or growth of cells in the brain. There are different types of brain tumors, some of which are benign and some of which are cancerous or malignant. Glioblastoma multiforme GBM is the most common invasive and actually the deadliest type of primary brain tumor in adults. The survival time after initial diagnosis is 12 to 15 months. This cancer has a relatively low prevalence but accounts for 2.5% of cancer deaths. One of the promising sites in which thiosemicarbazone compounds are being developed is their use against cancer. Their antitumor activity is very distinct and highly dependent on the biological type of tumor cells. The purpose of this study was to Evaluation of alternations in Akt gene expression in the T98G Glioblastoma cell line under treatment with thiosemicarbazone complexes (Cu).

Methods: In this study, thiosemicarbazone complexes (Cu) were prepared with 17.5 and 20μM concentrations. The T98G cell line was treated by Cu in 17.5 and 20μM concentrations after cell passage. Then RNA extraction and cDNA synthesis were performed and the expression of the Akt gene and GAPDH gene as the reference gene was investigated by Real-Time PCR, finally, the results were analyzed with Rest software.

Results: Our results confirmed that at both concentrations of 17.5 and 20μM a considerable gene expression decreasing observed after 24 hours of treatment. At 17.5 and 20μM concentrations, expression was detected 0/22 and 0/019 respectively. According to the expression level of the reference gene GPDH 1, the evidence showed a decrease in the expression of the gene under treatment with the thiosemicarbazones complexes Cu.

Conclusion: The results of cell line treatment with thiosemicarbazones complexes Cu of and comparison with the GPDH control gene showed that Cu can be effective in reducing the expression of the Akt gene as an oncogene. The results showed that these changes depended on the concentration of the drug because with increasing the concentration at a constant time, a greater decrease in gene expression was observed.

Keywords: Glioblastoma multiforme, thiosemicarbazones complexes Cu, AKT

Investigating the behavior of coronavirus 2019 in children's society (Review)

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Introduction: Coronavirus 2019 was declared an epidemic by the World Health Organization on March 11, 2020, and all activities around the world ceased. Since the virus was identified, initial data have focused primarily on adult infection, and there is little data on childhood infection. The present study examines the symptoms and how the disease occurs in children.

Methods: In this review, we searched for COVID-19, Infectious Diseases of Children, COVID-19 and Children in websites such as the Pub Med and Google Scholar. Finally, 17 papers in English and Persian were used for the regulation of the article.

Results: At the beginning of the outbreak, Covid 19 was thought to be an adult disease; However, according to new laboratory data, children are not immune to this disease. Unlike SARS and MERS, we have very little experience with children infected with the 2019 Corona virus; But according to research by Brandon et al., Covid 19, like SARS and Mercer, had milder symptoms and Less hospitalization, in children than in adults. Wang et al., In relation to children with Covid 19, concluded that; There were no severe cases and the most common symptom was fever, which was present in 65% of the children studied. Other symptoms such as cough, fatigue and diarrhea were less common and symptoms such as runny nose, vomiting and headache were rare. The lack of primary infection statistics of children was due to: low scope of children's activities in the community, different response of children's immune system to the virus, low underlying disease in children, non-smoking and low number of international trips among children.

Conclusion: The low number of children at the beginning does not mean that children are less susceptible to infection; The community of children is also affected by Covid 19. Children at any age are susceptible and no significant sex differences are observed. Obviously, more studies are needed to shape the characteristics of this disease in children.

Keywords: COVID-19, Infectious Diseases of Children, COVID-19 and Children

Investigating the effect of breast milk and formula on the growth and development of low birth weight infants (Review)

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Introduction: Breast milk or mother's milk is milk produced by mammary glands located in the breast of a human female to feed a child. Infant formula is a manufactured food designed and marketed for feeding to babies and infants under 12 months of age. The normal birth weight is 2,500 to 4,200 grams. If the baby weighs less than 2,500 grams after birth, the baby is called low birth weight (LBW). The aim of the study was to investigate the effect of breast milk and formula on the growth and development of infants (LBW).

Methods: We searched Pubmed ,Google scholar, Cochrane, SID and ISC databases with Breast milk, Infant formula,growth , low birth weight and infants . By searching these databases, only 16 articles were found in Pubmed and 40 articles were found in Google scholar. From 56 articles with investigating title we exclude 39 articles and with reading abstract we exclude 10 articles. Finally we include 7 articles in to the our study.

Results: Exclusive breastfeeding is the safest option for infants, especially premature infants with low birth weight (LBW). Breast milk increases levels (IGA) in low birth weight infants and reduces the frequency of sepsis, gastrointestinal diseases (small intestine and large intestine), premature retinopathy, lung and intestinal infections. A study showed that formula and complementary powders caused hard stools, wheezing, diarrhea, runny nose and colds, especially in infants under 4-6 months of age, thus reducing the proper growth process in infants.

Conclusion: According to the results, exclusive breastfeeding is the best option for infants (LBW), and it is best not to use dietary supplements and formula until 4-6 months of age if there is no barrier to breastfeeding. However, more studies are needed.

Keywords: Breast milk, Infant formula, growth , Low birth weight, infants

Investigating the effect of obesity factor on COVID-19 disease (Review)

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Introduction: With the outbreak of Covid 19 disease, we are witnessing an unprecedented pressure on the global health system. Obese people around the world are at risk for complications of Covid 19. The present study investigates the effect of obesity factor on Covid 19.

Methods: In this article, we searched for COVID-19, obesity, Covid 19 and obesity, obesity factors in websites such as the Pub Med and Google Scholar. Finally, 15 papers in English were used for the regulation of the review.

Results: Obese patients are at risk for exacerbating viral respiratory infections; However, the exact association of obesity with the severity of Covid 19 disease is unclear. Obesity during the 2009 H1N1 flu outbreak has been identified as an independent risk factor for influenza complications, Also, approximately 16% of MERS patients studied by Badawi et al. Were obese. Preliminary data suggest an increased risk of Covid 19 in obese individuals. Patients' BMA measurements have been performed by researchers, and concerns about BMA effects have been substantiated by preliminary data from Shenzhen (China) and New York (USA). According to research by Kai et al., Obesity increases the chances of developing severe Covid 19, and according to Chyngshyan et al., Obesity; Especially in men, it significantly increases the risk of severe pneumonia in Covid patients.

Conclusion: This study shows a high prevalence of obesity among hospitalized Covid patients; and the severity of the disease increased with increasing BMA. Obesity is a risk factor for the severity of Covid 19 that requires attention and preventive measures in susceptible individuals; But so far it has not been seriously evaluated.

Keywords: COVID-19, obesity, Covid 19 and obesity, obesity factors

Investigating the effects of red clover, turmeric, nettle and fennel plant extracts on osteoporosis (Review)

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Introduction: Osteoporosis is one of the most important and common diseases of the muscoskeletal system, especially in the elderly population. In Iran 1.1% of men and 2.7% of women above the age of 50 are suffering from osteoporosis. With the rise in the elderly population, the number of cases of osteoporosis is on the rise as well. Supplements and herbal compounds containing phytoestrogens as seen in plants such as red clover, turmeric, nettle and fennel have been shown to improve certain symptoms/complications of menopause such as osteoporosis. Therefore,The aim of this review study is to identify the effects of extracts of red clover, turmeric, nettle and fennel plants on osteoporosis.

Methods: In the following review article after searching key words “plants” “red clover” “turmeric” “nettle” “fennel” “osteoporosis” in credible English and Persian databases such as PubMed, Scopus Magiran, Scientific Information Database, web of science and google scholar; until the year 2020 without a date limit, a total of 104 papers were found. After a stepwise and more precise review, 15 papers were selected that were aligned with the purpose of the review study at hand.

Results: evaluation of the findings of selected studies indicated a reverse correlation between the changes in the amount of minerals within the body and osteoporosis as an increase in the level of minerals leads to a decline in the rate of osteoporosis. Accordingly, the findings here indicate the extracts of plants such as red clover, turmeric, nettle and fennel contain an abundance of minerals that are essential for the human body such as calcium, magnesium, manganese, copper, zinc, phosphorus, vitamins K-D-C, iron and herbal pseudo-hormonal isoflavones that by means of erythropoiesis and increasing the body’s energy level play an effective role against fatigue, muscle weakness, psychological issues, headache and anaemia as well as preventing a decrease in bone density, elimination of joint pain and increasing bone density.

Conclusion: the conclusions gathered by a thorough review of the effects of extracts of red clover, turmeric, nettle and fennel on osteoporosis show that certain attributes such as availability, containment of enormous amounts of nutrients, minerals and isoflavones seem to be effective on improvement of menopausal symptoms and physical/emotional distress. It is of importance to note that while beneficial, the use of such extracts may lead to complications as a result of interactions with various medications and herbs, therefore consultation with a physician or health care professional prior to using any supplements is required.

Keywords: red clover, nettle, turmeric, fennel, osteoporosis

Investigating the efficacy of three DNA-aptamer in targeted gene delivery to human prostate cancer cell lines (Research Paper)

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Introduction: Introduction: The selection of targeted and efficient carriers is still the major challenge of the drug and gene delivery to cells and tissues, so conjugating aptamer to nanoparticles has utilized broadly. According to results in biosensor, this study argued that several aptamers can improve a polycation gene delivery efficacy.

Methods: Materials and methods: We have investigated the effect of three DNA aptamers (AS1411, WY-5a, Sgs-8) conjugated to branched polyethylen imine (b-PEI; Mw ~25 kDa) with different combination for gene (plasmid) delivery to prostate cancer cell lines (DU145, PC3). The properties of aptamer-nanopolymers including size, surface charge density, morphology and cytotoxicity were evaluated.

Results: Results: The obtained results revealed that the aptamer-complexes had appropriate nano-scale size (141-175 nm) and positive charge density (20-28 mV). According to transfection results, the dual conjugation of aptamers (15%-10:5 AS:WY) to PEI increased gene delivery efficiency up to 3 fold in compare to unmodified PEI, as best combination. Surprisingly, triple aptamer arrangement not only reduced transfection ability but also showed cytotoxicity.

Conclusion: Conclusion: It is important to note, that the present evidence relied on aptamer and cell types. Overall, our results demonstrated potential synergic effect of aptamers for gene delivery with precise combination. Therefore, future research should be conducted with different aptamers, arrangements and cell types.

Keywords: Keywords: Aptamer; Gene delivery; Non-viral vector; Polyethylenimine, Prostate cancer.

Investigating the factors associated with vaginismus disorder: Systematic review (Review)

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Introduction: Introduction: Vaginismus is one of the most common sexual dysfunctions in women, which is characterized as a psychological phenomenon in the form of involuntary contraction of the pelvic floor muscles and the outer third of the vagina, which makes sex difficult or impossible. This involuntary contraction, in addition to intercourse, may be caused by the penetration of a finger or a dilator, the insertion of a speculum into the vagina during gynecological examination, depending on the actual pain or its prognosis. The aim of this Systematic review was to review the factors associated with vaginismus disorder.

Methods: Methods: This Systematic review was conducted with reference to medical science databases, pubmed, sid, science direct, magiran, google scholar and reviewed 20 articles from 2015 to 2019.

Results: Results: Although the etiology of vaginismus is unknown, studies suggest that it may be primarily physical, which may be the source of possible pain from abnormalities of the hymen, clitoris, and labia, and factors such as genital surgery, vaginal atrophy, and warts. Genital warts, endometriosis, or pelvic inflammatory disease can make sexual intercourse painful. It is also associated with psychological problems such as depression, anxiety, a history of traumatic sex, ignorance of physiology and sexual function, negative religious limitations and other psychological issues. Over the years, therapies have been used, including desensitization and the use of vaginal dilators, physiotherapy with or without feedback, sexual counseling, cognitive-behavioral therapy, and hypnosis. The prevalence of vaginismus in different societies is influenced by racial, cultural, socio-economic factors such as the strong value of a girl's virginity on the wedding night, the condemnation of sexual issues among single people. The prevalence of vaginismus in the general population of women is 0.4-8% and among outpatients to clinics is reported 17-5%.

Conclusion: Conclusion: Studies show that lack of sexual awareness or incorrect sexual education is an important factor in vaginismus. By examining this disorder in the social and cultural context, it is recommended to make the effectiveness of

sexual education programs to maintain the sexual health of people in the community as an important need.

Keywords: Keywords: Vaginismus, Sexual dysfunction, Vaginismus

Investigating the potential activity of carbonic anhydrase IX agents against cancer by moleculardocking simulation (Research Paper)

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Introduction: Carbonic anhydrase IX (CA IX) is a trans membrane protein that highly expressed in hypoxia tumor cells. Inhibition of CA IX isoenzyme by small molecule CA inhibitors such as sulfonamide derivatives has blocked tumor growth in multiple cancer models and CA IX is a promising target for cancer therapy

Methods: The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict mode of interaction between the best possible biological conformations of compounds in the active site of CA IX enzyme. The 2D structures of compounds were prepared by Chem Draw ultra 8.0 software and converted into 3D format by Hyper Chem7 using AM1 semi-empirical method. The compounds were docked into active site of CA IX (PDB ID: 5FL4) by MOE software. The best pose of compounds with the higher score was selected for ligand-target interaction analysis by LigX module in MOE software.

Results: The docking results showed a high docking score (-14.37 kcal/mol) for the most active compound of benzenesulfonamides in comparison to that of the least active compound (-12.97 kcal/mol) and also, CA IX enzyme is a zinc-dependent enzyme and zinc atom was coordinated with His 94, His 96 and His 119 as well as the NH2 group of the compounds.

Conclusion: The docking studies showed interaction mode of benzenesulfonamide derivatives with CAIX including zinc ion coordination, strong hydrophobic interactions and formation of hydrogen bond with benzenesulfonamide. The amine group of sulfonamide part as scaffold and the bulk groups as a hydrophobic part were key factors to improve inhibitory activity of CA IX and design more potent CA IX inhibitors for the therapeutic of cancer.

Keywords: cancer, carbonic anhydrase IX, molecular docking, benzenesulfonamides

Investigating the Relationship between Exon 1 Polymorphism of NOEY2 Gene in Women with Polycystic Ovary and Diabetes (Research Paper)

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Introduction: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. Although genetic factors have roles in PCOS, genes that are involved in the etiology of this syndrome are not studied comprehensively. The current study aimed to investigate the relationship between Exon 1 polymorphism of NOEYS2 gene in women with PCOS and diabetes.

Methods: this case-control study was conducted on 240 patients with PCOS and diabetes. Blood sample (1 cc) and genomic DNA of people were extracted and then, the primer was prepared for PCR based on the gene bank. DNA samples approved by Techazma Company were sequenced and the resulted sequences were analyzed by Chromas (version 2.4). Data were analyzed by Assotest method.

Results: polymorphism analysis showed that 5'UTR c.156G>A polymorphism in Exon 1 region of NOEY2 gene exists in people with diabetes, PCOS, and control samples while in people with diabetes-PCOS, no mutation is observed (100% hemology). On the other hand, 5'UTR c.207G+76 G>A polymorphism was observed in Exon 1 region in the control group.

Conclusion: in the investigation of Exon 1 polymorphism of NOEY2 gene, 5'UTR c.156G>A is related to PCOS and diabetes.

Keywords: polymorphism, genetic, NOEY2, PCOS

Investigating the relationship between infectious mononucleosis and increased risk of lymphoma cancer (Review)

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Introduction: Infectious mononucleosis (IM) is a common infection worldwide that affects about 95% of the world's population. The causative agent of this disease is the Epstein-Barr virus (EBV), which belongs to the Herpesviridae family. This virus can be transmitted through saliva and sex. There is considerable evidence that IM and its causative virus (EBV) can contribute to cancers such as lymphoma (Hodgkin's and non-Hodgkin's). Therefore, our study aims to investigate the relationship between a history of IM and an increased risk of lymphoma.

Methods: This review was conducted on Google Scholar, Pubmed, Scopus, and Sid databases from 2000 to 2020. Keywords Included infectious mononucleosis, lymphoma. A search of the databases with the title filter found 64 articles, of which 52 articles were deleted by reading the title and abstract. The imported articles included Persian and English articles.

Results: Finally, 12 articles were included in our study. In 7 articles, a positive relationship between the history of IM and Hodgkin's lymphoma (HL) was mentioned. A number of two articles also examined the relationship between IM and non-Hodgkin's lymphoma (NHL). In a 2013 study of 29 NHL tissue samples at Imam Khomeini Hospital in Ahvaz, Iran, it was found that 48% of the samples were significantly positive for EBV. One study also found that the risk of developing lymphoma after mononucleosis is more common in young people and the first two decades of life (with an average of 2/9 years later) so that the risk of developing lymphoma decreased with age.

Conclusion: Based on our study, we conclude that IM can be considered a risk factor for lymphoma. Therefore, considering the pathogenesis and transmission of this virus, further studies are needed on the risk of lymphoma in relatives of people with IM is recommended.

Keywords: Included infectious mononucleosis, lymphoma

Investigating the relationship between quality of life and mental health of older women (Review)

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1.

Introduction: The increasing trend of Iran's aging population and the associated phenomenon of aging with the occurrence of physical and mental disorders, has increased the need to determine the quality of life of this group. The quality of life of older women is more affected by various factors in terms of vulnerability. The aim of this study was to investigate the relationship between quality of life and mental health of older women.

Methods: The research is a review research and has been done by collecting materials from reputable articles on scientific sites such as sid, pubmed, etc.

Results: Findings show that measuring the quality of life and identifying the components of vulnerability of older women leads to planning, prevention and rehabilitation in order to improve their lives. The issue of quality of life is very important in different groups, especially the elderly who have special physical, mental and psychological conditions. Due to the increasing trend of the elderly population in the world, especially in developing countries and our country, and the phenomenon of aging with the occurrence of physical and mental disorders, the need to determine the quality of life of this age group has increased. The physical dimension of the quality of life of the elderly has a statistically significant relationship with such factors as education level, employment status, economic status, housing and the presence of disease.

Conclusion: In general, the results showed that due to the increase in the number of elderly, it is very important to pay attention to different dimensions of their quality of life, so measuring quality of life and identifying vulnerability of older women leads to planning, prevention and rehabilitation to improve their lives.

Keywords: old age, quality of life, mental health

Investigating the role of nutrition in the prevention of pancreatic cancer: A systematic review (Review)

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Introduction: Pancreatic cancer is one of the deadliest cancers and with the average survival of less than 6 months after diagnosis, it has the worst prognosis among cancers. Various hereditary and non-hereditary factors are involved in the formation of pancreatic cancer, among which important non-hereditary factors are nutrition and lifestyle. Therefore, nutrition should be considered as one of the important pillars in pancreatic cancer. The purpose of this systematic review is to investigate the role of nutrition in the prevention of pancreatic cancer.

Methods: In this study, which is a kind of systematic review, by reviewing authoritative books, related materials and concepts, collected and searched in selected scientific databases, including Iran medex, Google Scholar, Pubmed, SID with the keyword Prevention, pancreatic cancer , Diet, Patient were used and 88 articles were obtained. Among these articles, the full-text articles that were available and published in the last five years were further reviewed.

Results: The results showed that reducing the consumption of vegetables and fruits, increasing the intake of butter, cream, solid vegetable oil and consuming more than 5 cups of coffee during the day can increase the risk of pancreatic cancer. Curcumin (an active component of turmeric) can also play an effective role in preventing pancreatic cancer by reducing the concentration of cholesterol, fasting glucose and ultimately reducing the risk of liver fibrosis. Therefore, poor nutrition along with genetic background can affect the progression of inflammation, atrophy and eventually malignancy and pancreatic cancer.

Conclusion: The results of the study showed that nutritional factors such as increased fiber intake, reduced carbohydrate and fat intake can reduce the risk of pancreatic cancer. These results highlight the importance of following a healthy diet in the prevention of pancreatic cancer; Therefore, proper nutrition planning should be considered to prevent pancreatic cancer.

Keywords: Pancreatic cancer, nutrition, prevention

Investigation and Identification of the Role of LncRNAs Associated with ALS (Review)

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Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive paralysis disease characterized by the destruction of motor neurons in the brain and spinal cord. Typically, death from respiratory paralysis occurs within 3 to 5 years. The cause is unknown in 90 to 95% of cases, but physicians and researchers believe that both genetic and environmental factors are involved. The remaining 5 to 10 percent of cases are inherited from parents and there is currently no cure for ALS. Studies have shown that only about 1.2 percent of the genome is involved in protein encoding, and 98.8 percent of the sequences are non-coding sequences. It was shown that these types of non-coding RNAs are involved in processes such as pathology and showed a new horizon of expression regulation in cells in the transcription process.

Methods: Identification of differentially expressed genes.

Results: LncRNAs play a very important role in the normal functioning and maintenance of brain structures, studies have shown that LncRNAs are out of regulation in neurological disorders. Manipulation of gene expression and function of these molecules can play a key role in the treatment of diseases of the nervous system.

Conclusion: LncRNAs, or long non-coding RNAs, are significant cellular components that play important functional and regulatory roles within the cell. LncRNAs play a role in brain development, Genomic studies show that LncRNAs play a key role in human brain development. More than half of all LncRNAs are expressed in central nervous system cells (CNS), and their regulated expression is important in the development and function of the nervous system. Mature and developing neural systems exhibit specific regional, cellular, and subcellular concentrated expression profiles of LncRNAs that regulate vital functions, including neuronal stem cell maintenance (NCNs), neurogenesis, and Glycogenesis, homeostasis and synaptic binding are involved. In any case, whether the cell is replicating or not, maintaining genomic stability is of great importance, either by using DNA. Polymerases repair the mutations or kill the cell through apoptosis. However, accurate DNA repair is more limited in neurons that do not replicate. If

DNA damage is not repaired, nerve cells die due to neurodegenerative disorders. A number of pathogenic types of DNA repair proteins are associated with multiple neurological diseases. The purpose of this review study is to review the research conducted and finally to identify the types, role and function of LncRNAs in ALS, which is a growing disease in the global population. Which can play a key role in identifying, preventing and treating in the future.

Keywords: ALS- LncRNAs

Investigation of Chemical compounds and Antibacterial Activity of Capsicum Annum essential oil on Candida albicans and Pseudomonas aeruginosa Invitro (Research Paper)

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Introduction: In recent years Bacterial resistance to antimicrobial agents, is one of the important problems in Nosocomial infections. Capsicum Annum is highly valued for its therapeutic properties. The aim of this study was to identify the evaluation of Capsicum Annum essential oil antibacterial activity on Pseudomonas aeruginosa and Candida albicans in vitro.

Methods: In this paper,the Capsicum Annum essential oil,was extracted using Disk diffusion method was used to measure the diameter of the inhibition zone, and broth microdilution method was used to determine the minimum inhibitory concentration(MIC) and The components of the essential oil,were identified by gas chromatography/mass spectrometry(GC/MS)device.The minimum bactericidal concentration (MBC), was determined using tubes or wells, where no color hange was observed.

Results: The results showed that, 13 compounds, were identified in Capsicum Annum essential oil. The major compound of the essential oil was 2,3-dihydroxypropyl elaidate, 42.78% and oleic acid, 62.20% (42.63% of the total compounds). The diameter of inhibition zone for Pseudomonas aeruginosa ,Candida albicans were obtained 15, and 16 mm, respectively. MBC of Capsicum Annum essential oil for Pseudomonas aeruginosa and for Candida albicans, was 512mg/ml, respectively. However, increasing the concentration of Capsicum Annum essential oil reduced the diameter of the inhibition zone oncentration (512 mg / ml), prevented the growth of this yeast.

Conclusion: According to the results of this study, the Capsicum Annum essential oil has antibacterial effect which is higher in comparison with antibacterial effect of Tetracycline .The comparative results of the antimicrobial effect at concentrations of 1000 and 500mg / ml used of Capsicum Annum essential oil with tetracycline showed that 41/5% essential oil is more effective.On the other the maximum inhibitory diameter of Candida albicans yeast is lower at the highest concentration than the antibiotic amphotericin B.Thereforer Capsicum Annum essential oil can be presented as a new antimicrobial compound of the essential oil.

Keywords: Capsicum Annum ; Chemical composition; Antibacterial ;Essential Oils.

Investigation of HPV types prevalence by pyrosequencing method in cervical specimens (Research Paper)

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Introduction: Human papillomaviruses are small, double-stranded DNA viruses that infect the epithelium. More than 120 types of HPV have been identified. Their type's differences are based on the capsid L1 protein. Most HPV types infect the cutaneous epithelium and cause skin warts. About 40 HPV types infect the mucosal epithelium. These are classified according to their epidemiological association with cervical cancer. Infection with low-risk, or non-oncogenic types, such as types 6 and 11, can cause benign or low-risk cervical cell abnormalities, genital warts, and laryngeal papillomas. High-risk or carcinogenic HPV types act as carcinogens in cervical cancer and other anogenital cancers. High-risk types (currently including types 16 and 18, etc.) can cause low-grade abnormalities of cervical cells, high-grade abnormalities of pre-cancerous cervical cells, and anogenital cancers. High-risk types of HPV are diagnosed in 99% of cervical cancers. Type 16 is the cause of approximately 50% of cervical cancers worldwide, and types 16 and 18 together account for about 70% of cervical cancers. High-risk HPV infection is considered essential for the development of cervical cancer, but it alone is not enough to cause HPV infection in most women. In addition to cervical cancer, HPV infection is associated with less common anogenital cancers such as vulvar, vaginal, penile, and anal cancers. The association between HPV and non-genital cancers is less well established, but studies support a role for some pharyngeal cancers in this type of HPV. Cervical cancer is the second leading cause of cancer death in women. In this cancer, more than any other type of malignancy, the effects of prevention, early diagnosis and timely treatment on reducing mortality are evident. In the mid-1970s, the human papillomavirus (HPV) was proposed as the main etiology of cervical cancer. Various studies around the world have shown a strong association between HPV and precancerous and cancerous changes in epithelial cells. Because cell culture and serological methods are of little value in identifying the virus and its variants, the importance of molecular methods, including polymerase chain reaction (PCR), in definitive and early detection of the virus has become apparent. Cervical cancer is a type of cancer that starts in the cervix. The abnormal cells produced can spread to other parts of the body or attack them. There are usually no symptoms at the onset of the disease in the body, but subsequent symptoms may include vaginal bleeding, pelvic pain, or dyspareunia (any painful sexual activity called dyspareunia or painful marital activity). Cervical cancer usually progresses over a period of ten to twenty years following

precancerous changes. When HPV stays in the body for several years, it gradually turns some cells in the cervix into cancer cells, and these cells become more progressive. However, many people with human papillomavirus infections do not develop cervical cancer. It is suggested that sexual activity, age of first intercourse and number of sexual partners play an important role in causing this disease. How to diagnose cervical cancer: Diagnosis is made by screening the cervix with a Pap smear and then with a biopsy. Following the diagnosis, medical imaging is performed so that doctors can determine if it has spread. The HPV vaccine protects humans against two strains of the virus, and it is possible that the vaccine could prevent between 65 and 75 percent of cervical cancers. Because there is still a risk of cancer after treatment, it is usually recommended that cervical cells be sampled regularly. Symptoms of cervical cancer include: Pelvic pressure or pain, sciatica, bowel and bladder dysfunction, swelling of the legs.

Methods: In this study, after selecting patients according to the relevant protocol and completing the questionnaire form, 1047 samples of cervical cancer lesions were selected. DNA extraction from paraffin blocks was then performed by standard methods. The presence of HPV virus was detected by PCR. High-risk serotypes of the virus were investigated using pyrosequensing.

Results: Out of 1047 patients with cervical cancer, 160 were positive for HPV infection and 887 were negative. In other words, the prevalence of HPV infection in this population was 15%.

Conclusion: The findings of our study reinforce previous reports of a link between HPV and cervical cancer. Types 6, 11, 16 and 18 were also the most common.

Keywords: HPV, cervical cancer, PCR, Genotyping, Pyrosequencing

Investigation of probiotics on neonatal colic (Review)

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Introduction: Infantile colic describes excessive crying of unknown cause in otherwise well infants. Above 63%, of pediatricians surveyed, believed that the colic prevalence rate was >40% in the Middle East and North Africa region, which is greater than the 20% rate reported in worldwide surveys .Colic is traditionally defined by the Wessel's criteria of crying or fussing more than three hours of the day for more than three days of the week. A number of psychological, behavioural and biological components (food hypersensitivity, allergy or both; gut microflora and dysmotility) are thought to contribute to its manifestation . The aim of this systematic review is evaluates the efficacy and safety of prophylactic probiotics in preventing or reducing severity of infantile colic.

Methods: We found 24 clinical trial and Randomized Controlled Trial articles by searching in pubmed, Embase, Cochrane and SID from 2015 until 2019. The keywords were : neonatal colic, infant colic, probiotics, lactobacillus. 8 articles were excluded by checking their title, 3 articles were excluded by checking their abstracts and 2 articles were excluded by checking their full text. Finally , there were 11 articles related to our title and keywords.

Results: Finally,10 articles were included in the study. Six studies examined Lactobacillus reuteri DSM , one examined Lactobacillus rhamnosus(7), one examined Probiotic-Mixture. one studies began probiotics during pregnancy and continued administering them to the baby after birth . At another study one group received a sachet of probiotics per day along with a conventional treatment for two consecutive weeks. All studies were blinded, and at low risk of attrition and reporting bias. These Articles show that with the use of probiotics, the crying time is significantly reduced (68.4 min/day vs. 98.7 min/day; $p = 0.001$). According to the results of one examined Matricariae chamomilla L., Melissa officinalis L. and tyndallized Lactobacillus acidophilus , there was no significant difference between probiotic and control groups.

Conclusion: Evidence suggests that probiotics have a positive effect on neonatal colic. But more studies are needed to give a definitive opinion like examine other type of probiotics.

Keywords: neonatal colic, infant colic, probiotics, lactobacillus

Investigation of progesterone receptor gene expression changes in MCF-7 breast cancer cell line under simulated microgravity (Research Paper)

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Introduction: The living organisms on the surface of the earth are under influence of gravity force (1g) and any alteration on that, as experienced by astronauts during space travel, exhibit effects on cell functions by participation with biochemical pathways and gene expressions (1, 2). In some studies, it has been observed that changes in gravity, reduce the growth of some cancer cells, and alter the expression of some genes and cellular functions (3, 4). However, very little information is available on the effects of microgravity on the related gene expression. The aim of this study was to investigate the effect of simulated microgravity conditions on changes in progesterone receptor gene expression in MCF-7 breast cancer cell lines

Methods: MCF-7 breast cancer cell line has an oestrogen receptor, progesterone receptor but no human epidermal growth factor receptor 2 (5). The cells were cultured in DMEM medium, containing 10% sodium bicarbonate, supplemented with 10% FBS, and penicillin /streptomycin. All cell lines were incubated at 37°C in a humidified incubator with 5% CO2. The clinostat was employed for simulating microgravity. Cells were seeded at the culture tube and after the cells stick, tubes were completely filled by the medium. The rotation times were 24 and 72 hours and the device rotated by 30 rpm. Total RNA was isolated from the lysed cells and was subjected to reverse transcription using the qScript™cDNA Synthesis kit. To analysis the gene expression using Quantitative real-time RT-PCR, primer sequences were as follows: PR-total F (5'AGCCCACAATACAGCTTCGAG3'), PR-total R (5'TTTCGACCTCCAAGGACCAT3') (6). As a positive control, glyceraldehyde-3-phosphate dehydrogenase mRNA (GAPDH) was amplified in parallel with the primers: GAPDH F (5'ACGACCACTTTGTCAAGCTCAT3') and GAPDH R 5'TCCACCACCCTGTTGCTGTA3'). Cycling conditions were: 95º C for 30 sec; followed by 40 cycles of 95 ºC for 20 sec and 95 ºC for 40 sec. PCR melts curves were performed and changes in the fold number were calculated by using the 2ΔΔCt method. A statistical correlation was performed using independent samples t-test and $p<0.05$ was considered statistically significant.

Results: Results and discussion The concept of space cell biology is the study of the physical effects of space conditions such as microgravity on the cells and the answer to the question of whether gravity has direct effects on the cell and its function. It has been shown that in microgravity, the expression of some genes and protein levels produced in cultured cells or laboratory animals have been altered. However, very little information is available on the effects of simulated microgravity on gene expression. The study of these alterations would be beneficial to aid astronauts and improving the quality of human life. In order to apply microgravity on breast cancer cells, clinostat was applied and microgravity was simulated by rotating the system around the horizontal axis. After 24 and 72 hours of exposure to

microgravity conditions, total RNA was extracted from cells and RNA integrity was proved on the agarose gel. After that, the cDNA was constructed and a real-time PCR method was employed for investigation progesterone receptor gene alteration. The results have shown that no significant changes in gene expression were occurring. On the other hand, microgravity had no effect on the progesterone receptor gene on MCF-7 breast cancer cell lines.

Conclusion: Our results showed that simulated microgravity have not any effect on the progesterone receptor gene expression in MCF-7 cells at transcriptional levels, suggesting that there is a strong transcriptional control of this gene or optimization of microgravity application time may yield better results. Collectively, these results demonstrate that further studies may be necessary and investigation on protein level may yield other interesting results.

Keywords: progesterone receptor, microgravity, MCF-7 breast cancer cell lines

Investigation of the association of common polymorphism in two genes VDR and CYP27B1 with vitamin D3 serum level in an Iranian population with Alopecia Areata (Research Paper)

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Introduction: Importance of Vitamin D to body health has been known. These days, there are many authentic shreds of evidence related to the significance of vitamin D deficiency (values below 10 ng/mL) in various physiological disorders, especially immunological dysfunctions such as Alopecia areata. Vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) are two forms of vitamin D (calciferol). The accepted indicator of vitamin D3 sufficiency in humans is serum 25(OH)D3 level (defined as 30 ng/mL 100 ng/mL). This study is aimed to investigate the relationship between common variants in 2 vitamin D pathway gene (VDR and CYP27B1) and vitamin D3 serum level in patients with Alopecia Areata.

Methods: In this investigation, serum vitamin D3 metabolite levels were measured in 200 samples with Alopecia areata disease by Eliza method. Then, SNPs in VDR and CYP27B1 by the polymerase chain reaction (PCR)-sequencing method were analyzed.

Results: 42 variations in CYP27B1 and 21 variations in VDR were observed. A significant difference of Rs1544410 (odd ratio:7, p-value: 0.0005), and rs4646536 (odd ratio: 4.043 p-value: 0.0005) variants was found between the suffered and the controls.

Conclusion: The research revealed the significant association between the two polymorphisms, Rs1544410 (odd ratio:7, 95% CI, 1-8) and rs4646536 (odd ratio: 4.043, 95% CI, 3 -14.038) on VDR and CYP27B1 genes, respectively, with increased vitamin D3 insufficiency risk in the Iranian patients' population with Alopecia areata. Therefore, SNPs in the VDR and CYP27B1 genes can be considered a prognostic biomarker of Vitamin D3 deficiency risk.

Keywords: CYP27B1, VDR, Rs1544410, rs4646536

Investigation of the Effect of Phenytoin on the Ovary Differentiation and Expression of the Related Genes in Mouse Embryos (Research Paper)

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Introduction: Epilepsy is a disorder of the central nervous system (neurological disorder) in which the activity of nerve cells in the brain is disrupted and leads to seizures during which abnormal behavior, symptoms and feelings including loss of consciousness, occur. According to the World Health Organization, more than 50 million people worldwide are suffering from epilepsy (1,2,3). There are many drugs that are effective in treating the disease. Phenytoin is one of the most common drugs. The drug enters the cell through the sodium channel to modulate excitatory or inhibitory reactions and acts at different levels of synapses (4,5,6,7).

Methods: In this study, 2 groups of 7 balb / c mice were tested. The treatment group was treated with phenytoin before pregnancy until the birth of the infants and brain tissue sampling was performed. Finally, RNA was extracted from the target tissues, then their cDNA was synthesized and the expression of sox9, rspo1 and lif genes was measured using Real Time-RT PCR technique. Rest 2009 software was used to analyze the expression of genes. The gene network of these three genes was plotted using cytoscape software.

Results: In this study, expression changes according to statistical analysis in rspo1 and lif genes at the level of 0.05 are not significant, but sox9 gene has a 4-fold increase in expression. From the side effects of this drug phenytoin reduced sexual desire and reduced the quality of fertility in treated mice, so that the gestational age of treated mices were increased rather than control mice (About 5 to 7 days after delivery, the control mice gave birth to the treated mice). The number of fetuses born was less than the control group and the eating of rats in the treatment group was very high.

Conclusion: According to this results seems it is better to use an alternative drug that is safe and has fewer side effects than Phenytoin especially during pregnancy and lactation period.

Keywords: Phenytoin, ovary, , LIF, RSPO1, SOX9

Investigation of the effects of phenytoin on pregnancy in neonatal malformations (Systematic review) (Review)

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Introduction: Epilepsy is the most common neurological disorder in women of reproductive age. Phenytoin (PHT) is one of the antiepileptic drugs, which is frequently prescribed for epilepsy. Within the pregnancy, women experience physiological changes that have consequences for the pharmacokinetics and pharmacodynamics of the medications they take. Also, PHT can go through the placenta and concentrates on placental tissue. However, most women with epilepsy have normal pregnancy outcomes, but fetal anomalies and pregnancy complications are related to epilepsy and PHT use, therefore the current review aims to investigate the effect of PHT on pregnancy in neonatal malformations disorders.

Methods: This review was collected by searching within articles published at PubMed, ScienceDirect, Google Scholar, Scopus, Cochrane database systematic reviews from 1985 to 2020. The keywords were seizures, Phenytoin, neonatal, pregnancy. By searching this database, 57 articles were found, 11 of them were not related to investigating, and by reading abstracts were removed. All articles were chosen from English and Persian articles.

Results: Finally, 46 articles were included in the study. Waters et al. expressed most abnormal outcomes were reported with PHT and phenobarbital [1]. In terms of abnormal outcome (death and anomalies), phenobarbital was associated with the highest relative risk, PHT with intermediate relative risk. High third-trimester PHT levels may have a significant impact on newborn Sucking reflexes, development motor skills, malformations of the hands and feet, and the talipes deformity [2]. In other studies, the rate of fetal death and anomalies had a higher in the Offspring of women with epilepsy who were exposed to PHT [3, 4].

Conclusion: The basic spectrum of birth defects was confirmed and expanded upon by subsequent investigations into the teratogenicity of PHT include tracheoesophageal fistulas, cutaneous hemorrhages, and neural tube defects (NTDs). There is no safe dose that will supply therapeutic efficacy without the potential risk of inducing developmental or structural defects in the exposed infant. Based on the assumption, seizures should be adequately controlled during pregnancy. Therefore polytherapy must be avoided, in the management of women of reproductive age and whenever that is at risk of getting pregnant.

Keywords: Epilepsy, Phenytoin, Neonatal, Pregnancy

Investigation the effect of dendritic cells in improvement of pancreatic cancer (Systematic review) (Review)

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Introduction: Pancreatic cancer (PC) is one of the significant leading causes of cancer death and has the highest mortality rate worldwide. It is one of the most aggressive tumors with a poor prognosis. Dendritic cells (DCs) are occupational antigen-presenting cells that play a significant role in inducing and responding of primary immune responses that considering them as a vital goal in generating therapeutic immunity against cancers, so the aim of this study is investigating the effect of dendritic cells in improvement of pancreatic cancer.

Methods: This review article was performed within articles published at PubMed, Science direct, Google Scholar, SID and Cochrane until July 2020. The keywords were dendritic cells, pancreatic cancer and treatment. By searching this database; 161 articles were found, 92 of them by reading titles and abstracts were removed. 69 articles were selected under the inclusion criteria. All articles chosen from English and Persian articles.

Results: Finally 69 articles were included in the study. Suppressing PD-L1 in malignant cells during DC immunization could be a helpful tool in pancreatic cancer (PC). Increasing or decreasing the number of normal conventional dendritic cells (CDCs) in PC was an obvious strategy that could progress immune-based therapies. Vaccination with peptide-pulsed DCs in combination with poly-ICLC was safe and caused a measurable tumor specific T cell population in patients with advanced PC. DCs co-transfected with two mRNAs of tumor associated-antigens (TAA) MUC4 and survivin, compared to DCs transfected with a single mRNA encoding either MUC4 or surviving; induced a stronger response against the target cells in vitro of PC. DC-based immune therapy could be an appropriate strategy to remove pancreatic cancer stem cells (CSCs) in vitro and manufacture of DC loaded with CSCs associated antigens could present a modern and precious method for extracting the immune response to obliterate CSCs. DC vaccine loaded with Wilms' tumor gene 1 (WT1) peptides was a recent treatment for inactive metastatic PC. DC vaccination and combination therapy of CD40 agonist are considered as T cell-dependent anti-tumor immunotherapy in the treatment of pancreatic cancer. In addition, neutralizing TGF-β increased anti-tumor immunity of DCs against PC by regulating T cells, therefor the combination of DC–CIK immunotherapy and chemotherapy was beneficial in PC treatment.

Conclusion: It seems that modification of DCs with tumor antigen can influence T-cell activation and antitumor immune response. DCs-vaccination can increase potential of recovery in combined treatments aiming to destroy tumor cell, creating

innate and appropriate immune responses; however need to be more research done at this topic.

Keywords: Pancreatic cancer, Dendritic cell, Treatment

Investigation the effect of small interfering RNA (siRNA) in colorectal cancer therapy (Systematic review) (Review)

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Introduction: Colorectal cancer (CRC) is the third malignant cancer that is the main cause of death from cancers worldwide. So far, many treatments have been used to improve colorectal cancer, one of which is gene therapy. SiRNA is ribonucleic acids to length 18 to 21 that are encoded in the RISC protein complex to degrade their complementary mRNA, resulting in silencing after translation of the gene. It seems that treatment using SiRNA is a useful gene therapy in curing CRC, so the aim of this study is investigating the effect of small interfering RNA (siRNA) in colorectal cancer therapy.

Methods: This review article was performed within articles published at PubMed, Science direct, Google Scholar, SID and Cochrane until July 2020. The keywords were small interfering RNA OR siRNA, colorectal cancer, Nano liposome and treatment. By searching this database; 89 articles were found, 48 of them by reading titles and abstracts were removed, because they were not related. 41 articles were selected under the inclusion criteria.

Results: Finally 41 articles were included in the study. The results showed; Gene silencing of Rpt4 by using siRNA inhibited cell proliferation, reduced clonogenic survival and induced apoptosis in HCT-116 colon cancer cells. Using of nanoparticles combined with siRNA against CX3CL1 reduced the recruitment of Ly6c10 monocytes and improved outcome of anti VEGFR2 therapy in mouse CRCs. Tripolyphosphate (TPP) modified chitosan (CS) encoded with TGF-B1 inhibits siRNA (This factor TGFB1 increases tumorigenesis in advanced CRC). B7-H4 siRNA was able to inhibit proliferation, invasion, and migration of colorectal cancer cell line affectively through targeting CXCL12/CXCR4 and JAK2/STAT3. The siRNA against KRAS has been applied to prevent the proliferation of KRAS mutated CRC cells and to reduce the tumor growth in a xenograft mouse mode .The combined therapy of siRNA (PIK3CA + KRAS or Akt2 + KRAS) prepared a synergistic prevention of CRC cell proliferation and an increase in apoptosis.

Conclusion: It seems that siRNA could be used for a variety of goals such as the suppression of CRC cell proliferation and induction of cell apoptosis, overcoming multidrug resistance and prevention of CRC metastasis without making immune responses, however need to be more research done at this topic.

Keywords: Small interfering RNA (siRNA), Colorectal cancer, Nano liposome, Treatment

Investigation the Expression of Virulence genes (ctxA) of Clinical Strain Vibrio cholerae in BHI Broth Medium and the Caco-2 Cell Line (Research Paper)

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Introduction: Cholera is an infection of the small intestines caused by the bacterium Vibrio cholerae. It is a significant cause of an acute intestinal infection characterized via watery diarrhea that may cause dehydration and death, contaminating thousands of people each year worldwide and especially in developing countries. The major virulence factor produced by V. cholerae during infection is the cholera toxin. We examined the ctxA gene expression in medical eltor biotype and standard classic biotype ATCC14035 of V. cholerae in BHI broth medium and the Caco-2 cell line in the present study.

Methods: This study investigated the mRNA concentration of ctxA genes in four qualitative samples, including the ATCC14035 classic biotype and medical strain eltor biotype in two conditions: BHI broth medium and Caco-2 cell line interaction. The untreated population of Caco-2 cells used as control. The best MOI (Multiplicity of Infection) of two strain V. cholerae assessed by MTT assay, then adhesion and invasion test capacity determined to calculate the suitable population of bacteria. We analyze the number of adhesive bacteria in each biotype. Then we added such a number of bacterial populations in BHI broth and Caco-2 cell to having similar conditions based on this result. Total mRNA extraction and cDNA synthesis was performed with a specific kit. MRNA concentration calculated by quantitative Real-time PCR method on the using SYBR Green. Bacterial 16S rRNA used gene as internal control. All tests performed three-time repeat to reach the logical outcome.

Results: The best results with Caco-2 cell interaction were obtained at the MOI of 10:1.The adhesion rate of ATCC14035 classic biotype and eltor biotype to Caco-2 cells was 53% and 44%. Transcription of ctxA gene in eltor biotype and classic biotype interaction with Caco-2 cells was 10.4 and 10.5, respectively, that show a tenfold increase versus untreated Caco-2 cell (1.0) as control. In contrast, transcription of this gene in these two biotypes (eltor and classic) was 6.06 and 1.3 in the BHI broth medium. CtxA gene had different transcription in different conditions; we also observed the increase of transcription in interaction with Caco2 cell in both the ATCC14035 classic biotype and medical strain eltor biotype.

Conclusion: In conclusion, our study proposes that the expression of virulence genes (ctxA) was different in the BHI broth medium and the Caco-2 cell line interaction, also observed the increase of transcription in interaction with Caco-2 cell. This study may be valuable for understanding the relation of adenocarcinoma colorectal with the severity of cholera. More reviews on factors of these cells

involved in different gene expression of bacteria and hence the severity of disease are needed, especially in cancerous eukaryotic cells.

Keywords: BHI broth, Caco2 cell line, CtxA, Real-time PCR, Vibrio cholerae

Investigation the Expression of Virulence Genes (hlyA) of Clinical Strain Vibrio cholerae in BHI Broth Medium and the Caco-2 Cell Line (Research Paper)

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Introduction: Haemolysin (HlyA) is another critical toxin secreted by most Vibrio cholerae O1 and non-O1 strains. HlyA induces enterotoxicity, cytotoxicity, lysis of erythrocytes from several species, and cellular vacuolation. In the present study, we examined the expression of virulence genes (hlyA) of V. cholerae classic biotype ATCC14035 and medical eltor biotype in BHI broth medium and the Caco-2 cell line.

Methods: The expression of hlyA gene of ATCC14035 classic biotype and medical strain eltor biotype investigated everyone in two conditions, including Caco-2 cell interaction and BHI broth medium. The untreated population of Caco-2 cells used as control. The MTT test done to obtain the best MOI then adhesion and invasion test capacity were done to calculate the suitable population of bacteria. We analyze the number of adhesive bacteria in each biotype. Then we added such a number of bacterial populations in BHI broth and Caco-2 cell to having similar conditions based on this result. The RNA extraction and cDNA synthesis done with the specific kit. HlyA gene primers are confirmed by the PCR method. MRNA concentration of hlyA gene assessed using a Real-time PCR method on the using SYBR Green. Bacterial 16S rRNA gene used as the internal control. All tests done three-time repeat to reach the logical result and decrease the effect of errors due to unwanted mistakes.

Results: The best results with Caco-2 cell interaction were obtained at the MOI of 10:1.The adhesion rate of ATCC14035 classic biotype and eltor biotype to Caco-2 cells was 53% and 44%. Calculation of fold change in hlyA gene transcription shows an increase of about 14.9 and 8.39 in classic biotype and eltor biotype, respectively, with Caco-2 cell intraction versus untreated Caco-2 cell (1.0) as control. In contrast, this result in BHI broth medium was 2.11 and 2.02 in classic and eltor biotypes. HlyA gene had different transcription in different conditions; we also observed the increase of transcription in interaction with Caco-2 cell in both the ATCC14035 classic biotype and medical strain eltor biotype.

Conclusion: In conclusion, results showed that the expression of virulence genes (hlyA) was different in Caco-2 cell line interaction and the BHI broth medium. We also observed the increase of transcription in interaction with Caco-2 cells. This study may be valuable for understanding the relation of adenocarcinoma colorectal with the severity of cholera. More analyses on factors of these cells involved in

different gene expression of bacteria and hence the severity of disease are needed, especially in cancerous eukaryotic cells.

Keywords: BHI broth, Caco2 cell line, HlyA, Real Time PCR, Vibrio cholerae

Investigation the impact of breast milk on autism (Review)

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Introduction: Autism Spectrum Disorder (ASD) is a wide continuum of associated cognitive and neurobehavioral disorders, including impairments in socialization, impairments in verbal and nonverbal communication, and restricted and repetitive patterns of behaviors. The prevalence of ASD in 2014 was 1 per 80 cases which is increasing every year. The purpose of this study concerning the impact of breastfeeding on reducing the effects of autism in infants.

Methods: This review was performed within articles published at PubMed, Google scholar, sience direct and SID from 2000 to 2019. We achieved 153 results. 120 of them were not related with investigating and 23 of them by reading abstract were removed. Finally, 10 of them entered the study.

Results: The applied mathematics knowledge according to increasing the duration of breastfeeding resulted in a decrease in the risk of ASD. In kids with ASD decrease levels of lipoxin A4 and Glutathione within the plasma and increase levels of inflammatory cytokines in plasma that breast milk can be had a protective effect in these cases and elevates serum IGF quite bovine milk or infant formula. Breast milk also contains growth factors that play an important role in stimulating the maturation of the gastrointestinal tract. Often found in the ASD population are the physical signs of fatty acid deficiency; whereas breast milk especially colostrum is particularly rich in u-3 and u-6 fatty acids. The level of oxytocin can be provided by contact between the mother and the infant.

Conclusion: All studies on the effection of breastfeeding on autism we're incomplete because of a retrospective study and unreliable data, low statistical population, lack of control over all of the contributing factors to the study. To discover the effects of breastfeeding and it's the duration on the improve symptoms of autism, a study with high-risk populations is needed. It is better to examine the effects of breastfeeding by dividing patients into two groups(one group should be breastfed and the other group fed with other agents) and controlling other environmental factors for at least none year. Furthermore, raising ASD awareness among parents is valuable in helping autistic children.

Keywords: Autism, Autism spectrum disorder, Breastfeeding, Breast milk

Investigation the impact of parent`s smoking on Birth Weight (systematic review) (Review)

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Introduction: Introduction: Birth weight is the body weight of a baby at its birth and low birth weight is a term used to describe babies who are born weighing less than 2,500 grams. Maternal conditions during pregnancy can affect fetal health and conditions such as birth weight. Cigarette smoke, whether active or inactive, can affect human and fetal health, so the aim of this study is to investigating the effect of parent's smoking on birth weight.

Methods: Methods: This review article was performed within articles published at PubMed, Google Scholar, science direct and SID, from 2010 to 2019. The Key words were pregnancy, smoke, birth weight, parental, and their variations which were obtained from Mesh. By searching database, 41 articles were founded, 14 of them were not related with investigating and 7 of them by reading abstract were removed. One of the limitations was the lack of access to the full text of the articles.

Results: Results: Finally, 20 articles included in the study, all studies show significant decrease in the birth weight of neonatal in mothers smoking during pregnancy. In 10 articles which explaining the impact of father smoking during pregnancy on infant birth weight, 4 of them reported that it caused low birth weight while 6 of them don`t agree with this idea. In some of studies expressed, just being exposed to cigarette smoke can also affect the neonatal birth weight. Also, studies showed that the number of cigarettes per day effect on low birth weight.

Conclusion: Conclusions: It seems that women who smoke during pregnancy are expected to have low birth weight infants (LBW, & it; 2500g) which increases risk of infant mortality and morbidity. Little evidence is available regarding the effect of parental smoking on infant weight; therefore, it needs to be studied more. Pregnant women are advised not to smoke and also stay away from cigarette smoke to have normal birth weight infants.

Keywords: Keywords: Pregnancy, Smoke, Birth weight, Parental

Investigation the relationship between neonatal with acute kidney injury (AKI) and preterm birth (Review)

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Introduction: Acute kidney injury (AKI) is a life- threatening complication of infants admitted to the neonatal intensive care unit (NICU). The prevalence of AKI in neonates is about 6.3 to 8.4 around worldwide. Premature birth (gestational age<37 weeks) is one of the risk factors for AKI which is associated with poor nephron development. So the aim of this study investigation the relationship between neonatal with AKI and preterm birth.

Methods: This review was performed within articles published at PubMed, Google scholar, Cochrane and SID from 2010 to 2019. The keywords were acute kidney injury, preterm birth, and neonate. By searching this database, 42 articles were found, 22 of them were not related with investigating and 8 of them by reading abstract were removed. All articles chosen from English and Persian articles

Results: Finally 12 articles were included in the study. Some studies showed that the prevalence of AKI was more in infants that is less than 28 weeks of gestational age. Also an increased risk was observed even among term babies (37-38 weeks). A cross – sectional study that is performed on neonates admitted to the intensive care unit in US, examining the presence or absence of AKI and variables, such as data of birth, maternal age (preterm infant <28 weeks, very preterm 28 to<32 weeks, moderate to late preterm 32 to<37 weeks), and gender (male. Female), type of delivery (vaginal and cesarean) and birth weight(<1500 grams, 1500 to<2500 grams, > 2500grams) , the results showed that 70% of infants had AKI was son, and 90% of them weighed less than 1500 grams and also were preterm but some evidences indicated no significant association between the gestational age and AKI

Conclusion: While some articles have stated that gestational age can cause acute kidney injury but some articles suggested that there is no relationship between them so need to be more research done at this topic.

Keywords: Acute kidney injury, Preterm birth, Neonate

Is there a relation between nutritional intake and health status? (Review)

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Introduction: How much related do you think a person's health status is to the nutrition they consume? Is it possible to compare this with the relation between a car's conditions and the fuel that it intakes? We are made up of different organs. The building stone of these organs is cell. Which is the smallest unit that is responsible for our chemical and physical characteristicsOf course health status is as well one of our characteristics. So it extremely depends on our cells functioning. But what does our cells functioning depend on? Their action depends on molecules in their reach. The richer their nutritional source is the better they do their functions. Now we primarily understand the importance of nutrition in health status. Human body is like a really complicated device. Each organ is responsible for a special duty. And if there be even any small bug in this huge device, the whole device may stop working. Nutrition is not just responsible for growth and living but they also work in terms of confronting different damages and in terms of maintaining our health status. There are 20 different amino acids that are essential for the body. Human body is just able to make 10 of them so the other 10 must be eaten up and consumed in foods. No animal or plant protein source has all the 10 essential amino acid together. That is why our foods must be diverse and rich in different sources. Proteins and amino acids play different important roles in our body starting from DNA Replication, also including proteins that control cell division cycle and decide when to stop and start mitosis (such as CDK proteins); must of enzymes are protein as well. Foods are divided into 5 groups due to their nutritional content. All of these 5 groups are important: 1. Fats and sugars 2. Dairy products 3. Proteins 4. Carbohydrates 5. Fruits and vegetables. Also there is another grouping for nutrients: 1. Water 2. Minerals 3. Vitamins 4. Proteins 5. Fats 6. Carbohydrates. One big damage that our cells are confronting each day is the oxidative reactions that occur due to presence of highly activated radicals that damage cells and corrupt their functioning. Foods rich in antioxidants will help cells to stay wholesome and in this way we can prevent aging, wrinkles and even cancer.

Methods: To prove that nutrition has a big impact on health status, different experiments can be done. For example, we can bring some mice. One group will consume foods rich in different nutrition and the other will intake foods that lack in some nutritional sources. In this way you can examine the result of lack of each nutrition. Materials in this experiment are: mice, a place for separating mice, nutritional sources.

Results: Results show that the group which has received diverse nutritional sources live longer are happier and have more energy for daily activities; they are also better in shaped. Each organ works sharper in this group such as heart liver lungs and so on. The muscle weighs are higher in these mice. Bones are denser due to the higher calcium content and receiving enough vitamin D. they are also stronger in defending and fighting pathogens.

Conclusion: For sure it is obvious now if you want to maintain a healthy life you need to think again about your diet. your muscles weigh your bones density how your organs function depends on your nutritional intake. If you want to confront aging and improve your defense system you need to uptake more nutritionally valuable foods. Your heart will work better. Even the red blood cells will be safe and sound and contain enough iron. Your enzymes are made up of proteins that is why you need to consume them; you even need them for DNA replication. Your skin will stay younger if you receive enough antioxidants. Your neuron cells need minerals for sending and receiving signals and as you see even small functions in your body depend on the food you eat. If you want to live longer and healthier and receive valuable nutrition.

Keywords: Health, nutrition, organ, cells, function.

Is there any association between the MEF2A gene changes and Coronary Artery Disease? (Research Paper)

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Introduction: Introduction: Coronary artery disease (CAD) is a common multifactorial disease with a high rate of morbidity and mortality worldwide. The MEF2A gene transcription factor belongs to the myocyte enhancer factor-2 (MEF2) family and is involved in critical processes such as calcium-dependent signaling pathways and cardiac development. Although the variants of the MEF2A gene were studied in different CAD and myocardial infraction (MI) populations, the reality of this gene association with CAD is still unclear. This study reports the first in silico investigation on MEF2A variants.

Methods: Methods: All reported variants in CAD/MI patients were collected from eleven countries. Their pathogenicity and variants position conservation were surveyed by online prediction tools including Mutation-Taster, Polyphen-2, PROVEAN, SIFT, CADD, and GERP.

Results: Results: In silico analysis did not confirm the pathogenic effect of 21-bp deletion which was introduced as a monogenic cause of CAD. c.704C>A (p.S235Y), c.812C>G (p.P271R), c.836C>T (p.P279L) and c.848G>A (p.G283D) missenses, c.1315C>T (p.R439X) nonsense, and seven out-of-frame deletions were predicted as disease-causing variants.

Conclusion: Conclusion: Although some variants of the MEF2A gene affect protein structure, the MEF2A variation studies in CAD/MI patients and in silico analyses do not approve the association and pathogenicity of MEF2A variants in the familial/sporadic CAD.

Keywords: Coronary Artery Disease; MEF2A; in silico analysis

Is There Any Relationship Between Leukemia And Mothers' Breastfeeding In Iranian Children?: A systematic review of case-control studies (Review)

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Introduction: Leukemias are hematologic disorders that caused by mal-differentiation of immature white blood cells. This malignancy categorized by the cell type (lymphoid or myeloid) to acute forms, including acute myeloid leukemia and acute lymphoblastic leukemia, and chronic forms, including chronic lymphoblastic leukemia and chronic myeloid leukemia. According to WHO reports, acute lymphoblastic leukemia is the most common childhood malignancy in children under 15 years old. Although leukemia is a multifactorial disease, but its exact etiology has not been determined. Many studies have been shown the effect of breastfeeding on the prevention of some diseases such as infections, but the role of breastfeeding in preventing leukemia is not fully understood. In this study, we investigated the relationship between breastfeeding and leukemia in Iranian children.

Methods: A comprehensive search was conducted in electronic databases Embase, Pubmed, Scopus, Web of science, Sciencedirect and Magiran with the keywords “breastfeeding”, “leukemia” and all MeSH related words since 2000. The case-control studies have been done on the Iranian children that mentioned the duration of breastfeeding were included in this review.

Results: 1475 children were studied in this review. 668 case-patients and 807 control children were included in the study. The selected studies were done in Tehran, Shiraz, Hamedan, and Sistan and Baluchestan. All studies showed that breastfeeding was significantly associated with leukemia in children. Although most studies investigate the protective role of breastfeeding duration, but several studies mentioned that breastfeeding duration doesn't have any effect to protect children against leukemia. The most effective duration of breastfeeding was continuously up to 2 years. Male gender was observed as a risk factor for leukemia. Other risk factors such as family income, residence place, ABO blood group, and RH blood group were indicated in several studies, but the data was incomplete to analysis.

Conclusion: Regarding the protective and other beneficial roles of breastfeeding, it is recommended for adequate duration. Although more studies are necessary to determine the exact relationship between breastfeeding and leukemia.

Keywords: Breastfeeding, Iran, leukemia

Isolation and identification of bifidobacterium with probiotic potency from sheep intestines (Research Paper)

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Introduction: Probiotics are dietary supplements that contain live, non-pathogenic microorganisms that interact with the gastrointestinal microflora and directly with the immune system. Possible health effects of probiotics include modulating the immune system and exerting antibacterial and anti-mutagenic effects. The aim of this study was to isolate, identify and characterize Bifidobacterium strains from sheep intestines and also to determine some probiotic characteristics of the isolates.

Methods: In this study, a number of healthy-looking sheep were randomly selected and were sampled sterile from their intestines. After preparation of dilution and culture in MRS broth and agar medium, the samples were incubated in a CO2 incubator at 37 ° C for 24-72 hours. The bacteria were isolated and purified by phenotypic methods (gram staining, catalase test, biochemical tests including fermentation of carbohydrates and gas production from glucose). Then, these bacteria were studied based on initial probiotic indices including resistance to different concentrations of acid, bile salts and high salt concentrations. After the above experiments, three strains of Bifidobacterium from sheep intestine sample was isolated and the antimicrobial effect of these isolates on pathogenic bacteria was studied by using the well method. Then, one strain resistant to the high concentrations of acid, bile and salt that showed the best antimicrobial effect was identified by 16S rRNA gene sequencing.

Results: Among the isolated bacteria, five were gram-positive, anaerobic, non-spore forming, non-motile and catalase negative. They have various shapes including short, curved rods, club-shaped rods and bifurcated Y-shaped rods. Besides glucose, the isolated bacteria were able to utilize galactose, lactose, and usually, fructose as a carbon sources. The optimum growth temperature was 37-41 ° C, with maximum growth at 43-45 ° C and almost no growth at 25-28 ° C or below. The isolates were incapable of produce gas from glucose. The optimum pH for growth was 6-7 and from the above five isolates, three of the isolates were able to grow at pH 3-9 and also were resistant to bile salt with a concentration of 0.1-1.2 w / v and salt of 4.5 and 6.5%. All probiotic strains were able to inhibit the growth of pathogenic bacteria and Bifidobacterium bifidum had the maximum antibacterial effect.

Conclusion: Bifidobacterium is the common genus specified in sheep intestines. Therefore, probiotic bacteria isolated from sheep intestines have antimicrobial properties that can be utilized for industrial processes.

Keywords: Probiotic bacteria, Bifidobacterium, Intestinal flora, 16S rRNA, industrial processes

Isolation of Lactobacillus bacteria from traditional dairy products in Fars province and evaluation of its probiotic properties (Research Paper)

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Introduction: Probiotics are a group of beneficial bacteria with special properties that affect the general health of the human body, among other things, they are involved in the improvement of many diseases related to the gastrointestinal tract, such as diarrhea and constipation. Probiotics are used as dietary supplements and they are found in a variety of food products, including dairy products, also with continuous use, they create balance in the intestinal environment. The purpose of this study was to isolate, characterization and identify the probiotic properties of Lactobacillus bacteria, the most important bacteria in this group, from traditional milk and yogurt in Fars province, thereupon a number of isolated bacteria had probiotic properties.

Methods: In this study, different types of local milk and yogurt from different parts of the province were selected. After preparation of dilution and culture in MRS broth and agar, the samples were incubated in CO2 incubator at 37C for 24-72 hours. After that, conventional culture and identification methods were performed on bacteria based on their biochemical properties that including: fermentation of carbohydrates and gas production from glucose, gram staining, catalase test. Then, to investigate the probiotic properties of these bacteria including, pH resistance, high NaCl concentration and bile salts was evaluated. Seven strains of Lactobacillus bacteria were isolated. Also, the antimicrobial effect of these isolates on pathogenic bacteria was evaluated by well method. Therefore, one strain with the best characteristics was selected and other methods such as 16sRNA, PCR and gene sequencing were used for more accurate evaluation.

Results: As a result of these steps, gram-positive isolated lactobacilli were catalase negative, the best growth temperature was at 37 ° C, and were able to use the sugars arabinose, trehalose, xylose, sucrose, fructose, galactose, lactose, mannose, and mannitol, but strains Isolated Lactobacillus.plantarum was negative for inositol and rhamnose. In the case of probiotic tests, it was able to growth at a NaCL concentration of 4.5% and was resistant to bile salts and the optimum pH for growth was 5.5. Also all of them were able to inhibit the growth of pathogenic bacteria. The results of molecular tests showed the isolation of Lactobacillus.plantarum.

Conclusion: The use of probiotic products has a great impact on human health, as a result of this industry is expanding and progressing in the world and the need to study and isolate new bacteria with probiotic properties is very important and a

valuable contribution to this industry. The isolated lactobacillus.plantarum has significant probiotic properties that can be valuable for use in dietary supplements.

Keywords: Probiotic, Lactobacillus, Isolation, Dairy products

JAK/STAT signaling pathway involved in NK cell differentiation of CD117+ expressing progenitor cells (Research Paper)

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Introduction: Natural killer (NK) cells are the first body defensive line in destroying cancerous cells and virus infected cells. Reducing the activity of these cells can be associated with the incidence, deployment and spread of many cancers such as leukemia and autoimmune diseases. Also, hematopoietic stem cells transplantation is used to treat a wide range of patients such as hereditary anemia as well as blood malignant disorders. Previous in vitro studies have shown that using specific fundamental factors, bone marrow lineage hematopoietic stem cells can be differentiating into the NK cells. Notably, the use of NK cells for cell therapy relies on the availability of a great number of NK cells with optimal cytotoxic activity. Obtaining a large number of NK cells as well as the understanding and investigating the cellular and molecular mechanisms involved in stem cell differentiating is an important.

Methods: For this purpose, mononuclear cells (MNCs) were isolated from rat bone marrow by Ficoll-Hypaque gradient centrifugation and CD117+ cells were enriched by MACS method. In the following, CD117+ cells were treated in the presence of NK differential factors such as SCF (kit ligand), FLT3 and IL-15 for 21 days. At the end of culture period, the gene and protein expression of JAK and STAT were investigated by real-time PCR and western blotting, respectively.

Results: It was shown that NK cell differentiated cells were significantly expressed the gene and proteins JAK and STAT compared to CD117+ progenitor expressing cells

Conclusion: It was concluded that the CD117+ cells as hematopoietic progenitor cells could differentiate to NK cells. The current results also showed that the NK cell differentiation of CD117+ progenitor expressing cells could be through activation of JAK/STAT signaling pathway.

Keywords: NK cells, NK cell differentiation, CD177+ progenitor expressing cells, JAK/STAT signaling pathway

L-carnitine could contribute in NK cell differentiation of C-kit+ hematopoietic stem cells (Research Paper)

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Introduction: The ability of NK cells to eliminate tumor or virus-infected cells without prior sensitization has made them attractive for cell therapy. Obtaining a large number of NK cells is an important, although difficult task that underlies the most significant challenge to the development of successful NK cell adoptive transfer protocols. NK cells can be differentiated from hematopoietic stem cells and can be used for immunotherapy after a short- or long-term expansion in vitro with interleukins such as IL-2, IL-7 and IL-15. Unfortunately, the NK cell differentiation efficiency is low outside the body and a large number of cells lost during transplantation to target tissues. As a matter of fact, using components such as antioxidant which cause to differentiation rate and minimum cell injury must be notified. The aim of the present study was to investigate the in vitro effect of L-carnitine (LC) on NK cell differentiation of c-kit+ hematopoietic stem cells.

Methods: For this purpose, C-kit+ hematopoietic stem cells were enriched by MACS method. In the following, C-kit+ cells were divided in two groups; control group (C-kit+ cells cultured in the presence of NK cells differential factors such as SCF (kit ligand), FLT3 and IL-15) and experimental group (C-kit+ cells in the presence of NK cells differential factors and 0.2 mM l-carnitine). At the end of culture period (21 days), the protein expression of NK cells markers such as DX-5 and CD122 was investigated by western blotting.

Results: It was shown that the protein expression of NK cell markers DX-5 and CD122 NK were significantly increased in the experimental group in compared with control group.

Conclusion: It was concluded that the C-kit+ cells as hematopoietic progenitor cells could differentiate to NK cells. also, the significant role of l-carnitin in Nk cell differentiation of these cells was indicated by protein expression of DX-5 and CD122.

Keywords: NK cell differentiation, L-carnitin, C-kit+ hematopoietic stem cells, DX-5 and CD122 markers

LncRNA CCAT2 (Colon-cancer associated transcript-2) up-regulation in Iranian breast cancer patients (Research Paper)

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6.

Introduction: Long non-coding RNAs (LncRNAs) are a group of non-protein-coding RNAs, with more than 200 nucleotides in length, which consider as a new layer of biological regulation. Recent studies have shown that LncRNAs play key roles including proliferation, differentiation, migration and invasion in different cellular processes. CCAT2 (colon cancer–associated transcript-2) is a cellular LncRNA which shown in different types of malignancy such as gastric cancer, colorectal cancer and hepatocellular carcinoma.

Methods: Human sampels ,Breast Cancer blood specimens were collected from 30 patient women and 30 normal women . At first total RNA were extracted and after that they were removed to CDNA . At last the expresion level of CCAT2 (colon cancer–associated transcript-2) was quantified by Real Time PCR .

Results: LncRNA CCAT2 expression is significantly up-regulated in blood of patients with breast cancer comparing with normal blood specimens.

Conclusion: Up-regulation of LncRNA CCAT2 is shown in Iranian breast cancer patients that could correlate with aggressive disease progression and poor prognosis of breast cancer patients. LncRNA CCAT2 up-regulation might be involved in breast cancer carcinogenesis and become a potential future prognostic biomarker for breast cancer patients.

Keywords: Breast cancer/ Lnc RNA CCAT2/ Real Time PCR

Long Non-Coding RNAs in Thyroid Cancer: Implications for Pathogenesis, Diagnosis, and Therapy (Review)

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Introduction: Fibroblast growth factor, nerve growth factor neurotrophins, and insulin-like growth factor 1 are considered 3 families of growth factors that can be involved in the process of otic neurogenesis. In this respect, otic neurons can also be connected with mechanoreceptors in the ear, the hair cells (HCs), as well as the central nervous system. As a growth factor is combined with gene transfer technology, it can be used for hair cell regeneration. Gene therapy can be similarly employed to introduce genes into a system in order to induce the expression of genes for therapeutic agents, to replace defective genes, or to re-program supporting or surrounding cells to acquire the phenotype of lost or damaged cells in order to repair or regenerate the damaged tissue. The purpose of this review article was to investigate the epigenetic and growth factors involved in the differentiation pathway of embryonic stem cells (ESCs) into HCs and auditory neurons (ANs).

Methods: To this end, the databases of Directory of Open Access Journals, Google Scholar, PubMed (NLM), LISTA (EBSCO), as well as Web of Science were searched.

Results: : Given the results available in the related literature, the differentiation efficacy of ESCs toward the ANs and the HCs, the important role of growth factors, and 3 different strategies of application of miRNA, epigenetic regulation, and preparation of three-dimensional (3D) environments were suggested to be taken into consideration in order to improve these studies in the future. Furthermore, the role of epigenetic mechanisms and miRNA in this differentiation process became quite obvious; hence, the utilization of such procedures in the near future would be significant

Conclusion: Combining several techniques with a synergic effect (such as growth factor gene therapy and 3D environments) seemed to lead to obtaining the best results as a therapeutic strategy

Keywords: Growth factor · Three-dimensional culture system · Hearing loss · Hair cell regeneration · MicroRNAs

Long Term and High Dose Administration of Methylphenidate- Induced Cerebellar Morphological and Functional Damage in Adult Rats (Research Paper)

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Introduction: Stated in previous studies, physicians are typically prescribing Methylphenidate (MPH), commonly known as Ritalin, for children diagnosed with attention deficit hyperactivity disorder (ADHD). Nevertheless, researchers have not still understood mechanisms of this stimulant medication. Research has also found an association between apoptosis signaling pathway, neurological disorder, as well as treatment targets for neurological diseases. Therefore, the present study investigated effects of 3-week MPH oral (20 mg/kg) administration versus vehicle therapy on cerebellar morphology and function in adult male rats.

Methods: A total number of 30 adult male rats were randomly but equally divided into control and treatment groups. In fact, the treatment group was administered by MPH at doses of 20 mg/kg for 21 days and the control group only received saline solution. At the end of weeks 1, 2, and 3 following drug treatment, rotarod performance test was fulfilled. Once the study ended, tissues of the cerebellum were separated; then, inflammation parameters (i.e. tumor necrosis factor [TNF- α] and interleukin 1 beta [IL-1β]), pro-apoptotic genes (that is, bcl-2-associated X [bax] and caspase-8 proteins), along with histological changes were analyzed.

Results: According to the findings, MPH with the high dose of 20 mg/kg could remarkably enhance the levels of bax and caspase-8 genes compared with those in the control group ($p<0.05$). It should be noted that treatment with MPH could significantly increase TNF-α and IL-1β levels in isolated cerebellar cells ($p<0.05$). Moreover, 20 mg/kg of MPH decreased mean volumes of granular layer, white matter, as well as molecular layers. It also reduced the number of Purkinje cells compared with those in control rats. In addition, lower coordination movement was observed in the group receiving MPH.

Conclusion: Data analysis showed that chronic treatment with increased dose of MPH could possibly lead to neuroinflammation and neurodegeneration in the cerebellum of adult rats.

Keywords: Apoptosis, Inflammation, Cerebellum, Rat, MPH, Neurodegeneration

Main fetal surguries to treat Neural Tube Defects (NTDs): systematic review (Review)

Nafiseh Sami,[1,*]

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Introduction: Neural tube defects are birth defects of the brain, spine, or spinal cord. They happen in the first month of pregnancy, often before a woman even knows that she is pregnant. The two most common neural tube defects are spina bifida and anencephaly. There is no cure for neural tube defects. However, a variety of treatments can sometimes prevent further damage and help with complications. This systematic review discusses the main advances in fetal surgical therapy aiming to treat NTDs.

Methods: Researches on PubMed and google scholar database and Mehrsys Medical Library have been done and 55 articles were found since 2015. 12 aricles of which were included.

Results: Open fetal surgery reduces the rate of shunting, reverses hindbrain herniation, improves lower extremity function, and improves ambulation. The efficacy of open maternal-fetal surgery for myelomeningocele was proven by the Management of Myelomeningocele Study (MOMS) in 2003, and myelomeningocele is the first nonlethal disorder to be considered for fetal surgical treatment. An infant with myelomeningocele, in which the spinal cord is exposed, can have surgery to close the hole in the back before birth or within the first few days after birth. If an infant with spina bifida has hydrocephalus (excess fluid surrounding the brain), a surgeon can implant a shunt—a small hollow tube to drain fluid—to relieve pressure on the brain. Treating hydrocephalus can prevent problems such as blindness. People with encephaloceles are sometimes treated with surgery. During the surgery, the bulge of tissue is placed back into the skull. Surgery also may help to correct abnormalities in the skull and face. Surgery can separate the spinal cord from surrounding tissue in infants with tethered spinal cord. Finally, there is no treatment for anencephaly or iniencephaly. Infants with these conditions usually die shortly after birth.

Conclusion: Fetal surgery is offered at a few selected facilities with the required special expertise, multidisciplinary teams, and facilities to provide intensive care. It has been shown to improve short-term outcomes for the child, with the consequent risks of prematurity and maternal morbidity. As minimally invasive techniques and equipment evolve, the indications for fetal therapy are likely to expand.

Keywords: Fetal surgery, Neural Tube Defects, spina bifida, myelomeningocele

Malnutrition In the Elderly: A systematic review (Review)

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Introduction: Introduction: :The phenomenon of aging has become a universal subject and the world wide elderly population is continuously on the rise due to improvement of health-care services and an increase in an hopefully outlook towards life. Access to an appropriate nutrition has a profound impact on the state of health and the quality of life in the geriatric population. The elderly population is more vulnerable in terms of nutrition due to the use of a wide variety of medications, solitude, depression, lower quality of life, acute and chronic illnesses, hospitalization, nutritional insecurity, social, physiologic and health variations.The aim of the systematic review study at hand is to explore malnutrition in the elderly.

Methods: Methods: In this study, which is type of systematic review with evaluation of credible books, cases and concepts related to the subject, research in credible scientific information databases including SID, PubMed, google scholar, Iran medex, using keywords such as “elderly people” “diet” and “malnutrition” which yielded a total of 350 studies; among which those with a complete text that were published within the last 5 years were selected for further evaluation.

Results: Results: The results of the study indicated that the likelihood of the elderly to develop a form of malnutrition is alarmingly high. Solitude, isolation from society and being neglected by their children are some of the most important issues within the older population. At the same time, emotional distress and a rise in depressive disorders makes for further complications in maintaining a proper diet. Malnutrition in the elderly who possess an ever-changing immune system could possibly result in an uptick in acquired infections.

Conclusion: Conclusion: Considering the importance of the state of nutrition and its role in health and quality of life in the elderly, it seems that a continuous screening program and evaluation of diet in this population is of utmost value. Presentation of various healthy living teaching from younger ages in order to avoid the occurrence of many complications in seniors is one of the measures in prevention of malnutrition. Preventive measures include interventions in screening, on-time diagnosis, treatment and informative teachings.

Keywords: Elderly Population, Diet, Nutrition, Malnutrition, Disease

Marin algae in pharmaceutical industry (Review)

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Introduction: The bioactivity of Seaweed gives them a major role in the pharmaceutical section. They can be used as a prototype of new medicines by producing low and high molecular weight bioactive metabolites. Their synthesized bioactive compounds contain pigments (carotenoids, xanthophylls, chlorophyll and terpenoids), vitamins, saturated and polyunsaturated fatty acids, amino acids and antioxidants (polyphenols, alkaloids and halogenated compounds) and polysaccharides (agar, carrageenan, proteoglycans, alginate, laminaran, rhamnan sulfate, galactosyl glycerol and fucoidan).Many of these compounds were detected to have anti-bacterial, anti-fungal and various pharmaceutically-relevant activities that can treat cancer, diabetes, arthritis, acquired immune deficiency syndrome (AIDS), and other diseases.

Methods: Antimicrobial activity Seaweeds are known for their antimicrobial activity against different pathogens such as bacteria, fungi, protozoa and viruses. An example of marine flora that can produce an antibacterial agent that acts against shrimp pathogenic is Sargassum latifolium. While different brown, green and red algae such as Caulerpa sertularioides, species have an antiLeishmanial activity against Leishmania protozoa.In another study Sargassum oligocystum displayed antibacterial activity against Staphylococcus aureus (ATCC 25923), Staphylococcus epidermidis (ATCC 14990), Pseudomonas aeruginosa (ATCC 27853), and E. coli (ATCC 25922) when extracted in hot water rather than alcoholic extract. Another study shows that Sargassum oligocystum have remarkable antitumor activity against K562 and Daudi cell lines at concentrations 500 and 400 µg/ml of the algal extract. Different studies on brown algae genus Cystoseira showed that different species present different bioactivities against microbial community.

Results: Antioxidants Plant-originated secondary metabolites, such as antioxidant compounds, help in scavenging the accumulated free radicals in the human body that may result in DNA and cell damage. There is a positive correlation between the increase in algae phenolic content and antioxidant properties, because phenolic compounds act as electron donors and help in balancing the reactions created by free radicals in the body. Studies showed that different species of green, brown and red algae studied such as Laurencia snyderia, Acanthophora nayadiformis, Sargassum tenerrimum, and green algae Chaetomorpha Genus showed antioxidant activity. Several studies presented the fact that Sargassum sp. has the highest antioxidant activity compared to other tested algae. All Sargassum sp. and some other species like Canistrocarpus cervicornis and Cladophora sp., showed high antioxidant activity and they were rich in polyphenolic compounds. Furthermore, almost all the tested seaweeds contained hydroquinone, which is known as a skin whitening agent. A study showed that bioactivities among seaweeds and enzymes used for extraction were different. As an example,

Sargassum boveanumViscozymes and Sargassum boveanum-Alcalase showed high antioxidant activity, while most of the seaweeds extracted by Flavourzyme showed antimicrobial activity and therefore concluded that each seaweed species needs a specific enzyme to increase the yield of bioactive compounds. Cytotoxic compounds Studies show that specific compounds in marine algae such as fucoidans, laminarians, and terpenoids have cytotoxic traits against cancer cells by inhibiting their proliferation. Due to some recent research, cytotoxic activity against cancer and tumor cell lines, as well as immunomodulatory activity, has become one of the most important specificities of algae. The bioactive compounds in algal extracts were used in in treating toxic cells in human body such as cancer cells by following three different scenarios. They can cause necrosis (cell lysis), apoptosis (a genetically controlled form of cell death), and decrease in cell viability by stopping the division of actively growing cells. The latest research in this field are mainly focusing on elucidating the specific compounds that present such bioactivities. Also studying the synergistic effect of different bioactive compounds within algal extracts has attracted the interest of the scientific community, since the interactions between these substances increase the bioactive capacity. The cytotoxicity of these algal extracts activates an estrogen receptor-independent mechanism in breast cancer cells, which promote cell proliferation and tumor progression. The differences in the activity results between both studies may be a consequence of different solvents used for extraction, season and time of collection, and also different methods used.

Conclusion: Marin algae is an almost untapped pool consist of many compounds which have anti-bacterial, anti-fungal, algicidal, anti-viral, anti-protozoan and various pharmaceutically-relevant activities that can treat cancer, diabetes, arthritis, acquired immune deficiency syndrome (AIDS), and other diseases.

Keywords: Marin algae, Antimicrobial activity, Antioxidants, Cytotoxic compounds

Mast cells improve functional recovery of transected peripheral nerve: A novel preliminary study (Research Paper)

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Introduction: Employment of regenerative properties of cells at the service of nerve repair has been initiated during recent decades. Effects of local transplantation of bone marrow-derived mast cells on peripheral nerve regeneration were studied using a rat sciatic nerve transection model

Methods: A 10-mm sciatic nerve defect was bridged using a conduit chitosan-based hybrid conduit filled with BMMCs in BMMC group. In positive control group (Pos), the conduit was filled with phosphate-buffered saline alone. The regenerated nerve fibers were studied within 12 weeks after surgery. In sham-operated group, the sciatic nerve was only exposed and manipulated. In negative control (Neg) a 10-mm sciatic nerve defect was created and the nerve stumps were sutured to the adjacent muscles. The regenerated nerve fibers were studied functionally, biomechanically, histologically and immunohiscochemically

Results: Functional and biomechanical studies confirmed faster recovery of regenerated axons in BMMCs transplanted animals compared to Pos group ($p < 0.05$). Morphometric indices of the regenerated fibers showed that the number and diameter of the myelinated fibers were significantly higher in BMMCs transplanted animals than in Pos group ($p < 0.05$). In immunohistochemistry, location of reactions to S- 100 in BMMCs transplanted animals was clearly more positive than that in Pos group.

Conclusion: BMMCs transplantation could be considered as a readily accessible source of cells that could improve functional recovery of transected sciatic nerve.

Keywords: Nerve regeneration BMMCs Chitosan conduit

maternal vitamin d deficiency and risk of childhood epilepsy (Review)

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Introduction: epilepsy is an abnormality of the nervous system, which may caused by fetal stimulation.maternal vitamin d deficiency is one of the factors associated with childhood epilepsy.our goal is to investigate the association between vitamin d deficiency and neonatal epilepsy.

Methods: we did a search with the keywords "maternal vitamin d deficiency" AND "childhood epilepsy " in Google Scholar, PubMed and SID databases. about 100 articles were found which just 15 of them were related to our topic.finally, we included case control, cross sectional and cohort studies in our research.

Results: vitamin d under 35 mg/ml considered as a vitamin d deficiency.according to the articles, vitamin d deficiency in pregnant mothers can effect on fetus neurologic growing and cause diseases like epilepsy in childhood. maternal vitamin d has meaningful relation with fetus vitamin d. nationality has no association with the amount of vitamin d.

Conclusion: these studies did not fully confirm the association between vitamin d deficiency and neonatal epilepsy, but it is recommended that pregnant women be informed of their vitamin d levels before pregnancy.

Keywords: neonatal epilepsy, vitamin d deficiency, pregnant women

Menopause and cardiovascular disease: A systematic review (Review)

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Introduction: In the last few decades, the elderly population has outnumbered the young, while women spend nearly a third of their lives after menopause. From the perspective of global health, menopausal complications and problems are considered very important in women. Menopause and its hormonal changes have a significant impact on the overall health of women, especially the health of the cardiovascular system, so that the death rate of women due to cardiovascular disease is twice as high as that of malignant diseases. The aim of this study was to evaluate the risk factors and cardiovascular disorders in postmenopausal women.

Methods: In this study, which is a kind of systematic review, by reviewing valid books, related materials and concepts, collected and categorized and searching in selected scientific databases, including Iran medex, Google Scholar, Pubmed, SID with the keywords menopause women, cardiovascular disease , Risk factor, complication was used and 350 articles were obtained. Among these articles, the full-text articles that were available and published in the last five years received further scrutiny.

Results: The results of this study showed that menopause has a significant effect on the incidence of cardiovascular disease; As the production of estrogen decreases, the level of serum lipids and cholesterol increases, and consequently the dilation and elasticity of blood vessels decreases, and the function of the heart in pumping blood to the organs is impaired. Menopausal hot flashes can also lead to cardiovascular disease by increasing vascular obstruction and increased vascular endothelial disorders. In addition to hormonal changes, factors such as waist size, blood pressure, smoking, physical activity and financial stress during menopause also affect heart disease.

Conclusion: This study showed that menopause endangers cardiovascular health in women. Therefore, preventive measures in late menstruation and early menopause can be effective in reducing cardiovascular disease in postmenopausal women. Preventive measures require intervention in screening, timely identification, treatment, education and proper information. To improve lifestyles, people can change their performance by increasing their awareness through mass media.

Keywords: Menopause, cardiovascular disease, side effects, risk factor

Mental health of medical staff, patients and the elderly people in countries affected by the Covid-19 pandemic (Review)

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Introduction: Coronaviridae belongs to the family of RNA- sense positive viruses, enveloped (lipid coatings) and spherical viruses, which in recent years have seen the outbreak of viruses of this family, such as Severe Acute Respiratory Syndrome (SARS) in 2003, which causes pneumonia and advanced respiratory failure, and over the course of 2012 we saw the outbreak of Middle East Respiratory Syndrome (MERS) which like SARS, involved the host respiratory tract. In December 2019, an outbreak of an unknown pathogen intensified in Wuhan City, Hubei Province, China, so that from December 18 to 29, five patients were hospitalized, one of whom died. This trend gradually escalated until researchers were able to isolate the causative agent of the disease, identifying it and finding that a virus from the coronavirus family is the cause of these diseases and deaths, and on February 11, 2020, the World Health Organization (WHO) He called the virus COVID-19. Phylogenetic studies on this pathogenic virus have shown that it is a beta-coronavirus and is closely related to bat coronaviruses, which attracted the attention of the general public and experts to bats. On March 11 this year, the WHO declared the outbreak of COVID-19 a pandemic. Despite the global prevalence of this deadly virus, no definitive drug or treatment has been found for it. The COVID-19 pandemic has profound effects on health, the economy, people's lifestyles, mental health, and so on in countries affected by the virus worldwide. In recent years, studies aimed at investigating the impact of the prevalence of SARS on the mental health of people with the disease showed a negative impact on people with the virus. Among the psychological effects that COVID-19 has had on the world and in studies that have been proven in various countries such as China, Japan, the Arab countries of the Persian Gulf, Africa, etc., we can stress and anxiety, Concerns and... Pointed out. The purpose of this review study is to review the studies conducted focusing on the impact of the global prevalence of COVID-19 on the mental health of different individuals in the community affected by this disease according to their occupation, age, etc.

Methods: At first, we used comprehensive keywords such as COVID-19, Mental Health, on Science Direct, Google Scholar, and more. In the next step, we used the words and, or between the keywords to extract articles that are completely related to the subject under study and writing this review article entered the further review process.

Results: A study in China examined the level of anxiety, stress and other psychological problems of medical staff. In this study, the statistical population surveyed was 1257 people, including 493 physicians and 764 nurses in various hospitals, of which 34 were reported. They have been at work since the beginning of the outbreak of COVID-19 and have been in contact with those infected with the

virus, and the results showed that 50.4% had symptoms of depression, 71.5% had distress, 34% had sleep disturbance, and finally, 44.6% had anxiety symptoms. A noteworthy point in this study is the recording of more severe symptoms in the medical staff of Wuhan hospitals. The results of a study published in the Arab and African countries known as the MENA region include Algeria, Egypt, the United Arab Emirates, Sudan, Morocco, Tunisia, Lebanon, Jordan, Saudi Arabia, Qatar and several other countries. With the global outbreak of COVID-19 due to the lack of adequate support for the elderly, this particular group is under pressure in terms of mental health and needs the participation and support of relevant governmental and non-governmental organizations. In a study conducted in China among 205 people in 3 groups, and we refer to 2 groups of them in this section. The first group consisted of patients with COVID-19 (n = 57) and the second group consisted of quarantine subjects (n = 50) who assessed depression and anxiety among these individuals. 36.8% of Covid-19 patients, ie 21 people, did not show any signs of depression, but on the other hand, in quarantined people, this figure had reached 70%, ie 35 people. The incidence of severe depressive symptoms was 19.3% in patients with Covid-19 and only 4% in quarantined patients. In 54.4% of patients, no symptoms of anxiety were observed, and in 72% of quarantined patients, no symptoms of severe anxiety were observed. Finally, 32% of patients showed severe symptoms of anxiety and only 2% of quarantined patients showed severe symptoms of anxiety. Researchers in this study have linked the degree of sensitivity of people to mental health injuries to gender, social support, and so on.

Conclusion: Carrying out similar studies in Iran in order to accurately assess and inform the mental health of compatriots, and in this regard, conducting counseling activities through the national media, telephone calls with people at risk of mental injury in order to encourage them, efforts to Increasing the awareness of the country's population on the easy control of this disease with the measures recommended by the Ministry of Health and reducing the mental injuries that follow can help control or reduce mental injuries and increase people's mental health.

Keywords: Medical staff, Patients, Elderly people, Pandemic, COVID-19

Metabolic syndrome components among asthmatic males and females (Research Paper)

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Introduction: Asthma is one of the most common major non-communicable diseases and metabolic syndrome (MetS) prevalence is high in the population of asthma patients. Indeed, MetS impairs lung function, but the details of interaction have remained mostly unknown. The MetS is a group of risk factors diagnosed by a co-occurrence of three out of five risk factors of the high waist circumference (WC) which represents central obesity, Blood pressure (BP), Fasting blood sugar (FBS), Serum triglycerides (TG), and low high-density lipoprotein cholesterol (HDL). Recently, an emerging increased prevalence of MetS risk factors among Iranians, especially among the Azarbaijani population has been reported. Considering the possibility of different roles of MetS components in interaction with asthma and gender of affected patients, this study aimed to analyze and compare the frequencies of MetS components among asthmatic male and female patients, which was supported financially by the National Institute for Medical Research Development of IRAN (Code: 957667).

Methods: Attended patients to the office of pulmonary specialist affiliated to Tuberculosis and Lung Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran, were examined and asthmatic cases diagnosed by spirometry tests were included in the study. Risk levels of MetS components were identified following IDF definition: WC (man>102cm, woman>88cm), BP (≥130/85 mmHg, or on the treatment of previously diagnosed hypertension), FBS (≥100 mg/dl, or on the treatment of previously diagnosed type 2 diabetes mellitus), TG (>150mg/dl), and HDL (man<40 mg/dl and woman<50 mg/dl) or on the treatment of previously diagnosed dyslipidemia. Research protocols were approved by the medical ethics committee of the research council of the National Institute for Medical Research Development, Tehran, Iran (IR-NIMAD-REC-1396-032). All participants signed informed consent for participation. Statistical analysis of the collected data was done using SPSS version 26.

Results: Among 588 asthmatic patients, risk levels of WC and BP were observed in 63.3% and 18.4% respectively. Also, 82.3% of females and 36.5% of males had a risk level of WC, and the difference of these frequencies was significant

(P<0.001). Furthermore, the frequency of risk levels of BP in females (23%) was significantly higher (P=0.001) in comparison with the frequency in males (11.9%). However, smoking, drug abuse, and drinking frequencies were significantly higher (P<0.001) among males. There was no significant difference between male and female patients in the frequency of risk levels of other MetS components such as TG (males: 8.2%, females: 9.6%), HDL (males: 7.4%, females: 9.0%), and FBS (males: 6.6%, females: 7.8%).

Conclusion: Elevated risk levels of waist circumstance and blood pressure were observed among asthmatic patients. In comparison with asthmatic males, risk levels of waist circumference and blood pressure were significantly higher among females with asthma disease.

Keywords: Asthma, Metabolic syndrome, Disease-disease interaction, Central obesity, Blood pressure.

Metagenomics Studies in Diagnosis and Treatment of Prostate Cancer (Review)

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Introduction: The mutation occurred in prostate cell genes lead to abnormal prostate proliferation and cancer. Prostate cancer is one of the most common cancers among men, and its prevalence in Iran is increasing with the age of men. About 16% of the world's cancers caused by microbes that live in the human body. Impaired population balance of symbiosis microbes that live in the human reproductive ecosystem is associated with the development of prostate cancer. In this review, we intend to interrogate the role of metagenomics studies in the diagnosis and treatment of prostate cancer.

Methods: literature review

Results: The microbial imbalance in the genital tract of men may affect prostate health. Based on Next Generation Sequencing-generated data, proteobacteria phylum (Escherichia, Pseudomonas, and Acidovorax genera) most frequently has been detected in a prostate cancer sample, which induces mutation in the prostate cells and causes cancer.

Conclusion: With the advent of metagenomics science, the genome sequences of the microbiota of the human body became known. Therefore, it was possible to identify a higher range of microbiome changes in prostate cancer tissue through the Next Generation Technique, and this will have good consequences in personalized medicine. Many kinds of researches are underway to investigate and identify novel microbes in prostate cancer tissue.

Keywords: Prostate Cancer-Metagenomics-Next Generation Sequencing-Microbiome

Meteorological conditions and pollen allergenicity (Review)

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Introduction: It is estimated that about 40% of people have some kind of allergy. The reason for this increase is attributed to environmental and climate change. Many airborne pollen grains released by tree, grass, and weed species can cause pollinosis in susceptible individuals with symptoms such as watery eyes, eye irritation, runny nose, skin irritations, dry cough, and sneezing. Meteorological factors such as temperature, humidity, rainfall can affect the release of allergens from pollen grains and its allergenic content. This review is aiming at producing relevant data that have been published on the influence of meteorological conditions on the allergenic potential of pollen grains.

Methods: In this paper, we conducted a scientific databases search using nearly 50 related scientific terms and keywords and summarized more than 20 scientific articles related to the relationship between Meteorological factors and the potential of pollen allergenicity.

Results: Pollen allergenicity is associated with allergen concentrations. Some studies have reported an increase in the pollen allergen content produced by plants grown at high temperatures and in carbon dioxide-rich atmospheres. Studies have also shown that the concentrations of the main allergen in ragweed (Ambrosia artemisiifolia), Amb a 1, increase in carbon dioxide-rich atmospheres. Global warming and rising temperatures are causing severe drought stress, especially in urban areas. In ragweed, a major allergenic species, the expression of allergenic proteins is upregulated under drought conditions. Also in a species of birch (Betul apendula), pollens from trees grown in the south (higher temperature) had the highest amount of allergenic proteins. The main allergen of Birch, Bet v 1, shows significantly more severe allergenicity in trees grown at higher temperatures. In another species of birch (Betula pubescens), a higher average daily temperature is associated with increased levels of the major allergen in birch pollen (Bet v 1). However, some studies have reported a negative relationship between Bet v 1 allergen content and temperature increase. Recent molecular studies have shown the temperature-dependent expression of the gene encoding the allergen Bet v 1. This study showed that high temperatures positively regulate the promoter activity of Bet V 1 gene. however, Recent studies indicate regional and year-to-year differences in the release of the Bet v 1 allergen from birch pollen. During the natural pollination period, mature pollen grains are dehydrated when released by the anthers at the time of dispersal. When pollen grains come in contact with a wet surface, they absorb water and undergo metabolic and ultrastructural changes. Pollen allergens are located in the pollen walls or cytoplasm and are rapidly released when pollen grains come in contact with the mucous membranes of the mouth, nose, and conjunctiva and causing pollen allergy symptoms in sensitive patients. Sometimes cytoplasmic allergens are located in the membrane around the starch grains, when pollen grains burst under osmotic stress, they are released into

the atmosphere and can form a breathable allergenic aerosol. Birch pollen can explode in high humidity conditions and release an aerosol from the cytoplasmic components of the pollen (in the range of 30 μnm to 4 μm), which contains the allergen Bet v 1. Under high humidity conditions, about 65% of pollen grains form a 300 micrometer pollen tube before rupture and release of their cytoplasmic contents. The released particles form a very fine aerosol that can penetrate the lower respiratory tract and cause allergy symptoms. In 1985, a new link between thunderstorms and asthma outbreaks was identified, described as thunderstorm asthma. During thunderstorms, pollen grains may release some of their contents including starch granules containing an allergen (0.5-2.5 microns) or other cytoplasmic components into the atmosphere after bursting by osmotic shock. These starch granules can penetrate the lower respiratory tract and provoke asthma symptoms. Thunderstorm asthma is limited to late spring or summer when high levels of airborne pollen grains are present in the atmosphere.

Conclusion: In conclusion, Humidity and temperature seem to be two important factors affecting the release of allergens from pollen grain and its allergenic content. In light of this review, there is a growing body of evidence supporting the effect of meteorological conditions on the allergenic potential of pollen grains.

Keywords: allergy, pollen, pollinosis, Meteorological factors, allergen

MicroRNA regulation of allergic inflammation and asthma in TNF pathway (Research Paper)

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Introduction: Allergic asthma is an inflammatory disease of the airways characterized by recurrent episodes of wheezing and bronchoconstriction which frequently occur together. Chronic inflammation may finally lead to structural damage followed by airway remodeling. Diagnosis and treatment progression have key role in exploration of biomarkers for allergic rhinitis and allergic asthma. A novel group of gene expression regulators is a class of small non-coding RNAs of 18-24 nucleotides in length, function to post transcriptionally regulate protein expression termed microRNAs (miRNAs). miRNAs can cause gene silencing through degradation of target mRNAs or blocking of translation. Dysregulated expression of miRNAs has been shown in various human diseases, such allergic asthma. Although studies of miRNAs in inflammatory upper airway diseases are relatively new and few, emerging evidence implicates an involvement of miRNAs in shaping the inflammation pattern in upper airways.so this study aims to investigate the relationship between allergic asthma and miRNAs in associated pathways.

Methods: By using mirbase, HMDD and miRdSNP, miRNA properties were obtained. The miRTarBase, MIRWALK2.0, TargetScan, DIANA Tools target genes were identified. Venn diagram used to identify common target genes between MiRNAs. Using DAVID and KEGG, signal paths were obtained and the pathways associated with allergic asthmacer were interpreted. The gene network was obtained through GENE MANIA.

Results: The result demonstrated that mir199a, mir-27a, mir-374b and mir-374a inhibit Ras by blocking Raf-1,MEK1/2 which active ERK,SRF and c-fos through phosphorylation in MAPK and Gap junction pathways. Mentioned microRNAs prevent allergic asthma by inhibiting (IL1b-IL6-IL15-lif-tnf) by blocking MKK4/7, JUNK1/2 in TNF pathway .

Conclusion: TNF pathway has been implicated in many aspect of the airway pathology allergic asthma in which mir199a, mir-27a,mir-374b and mir-374a prevent inflammation and allergic reaction by inhibiting leukocyte activation and inflammatory cytokines.so miRNAs can be act as potential biomarkers in TNF pathway by inhibiting allergic asthma progression.

Keywords: Allergic asthma, MAPK pathway , MicroRNA, TNF pathway

MicroRNA-29 family has high affinity to SARS-CoV-2 genome: an in silico analysis (Research Paper)

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Introduction: Coronavirus disease 2019 (COVID-19) caused by a novel betacoronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has attracted top health concerns worldwide within a few months after appearance. COVID 19 as a single-stranded positive-sense RNA genome with the size of 26 – 32 kilobases (kb) in length, have the largest known genomes among all known RNA viruses. The virus genome possesses a 5′ cap structure together with a 3′ poly A tail, authorized act as mRNA molecules to translate its proteins. About two-thirds of the genome at 5´ end occupied by the replicase gene, which encoded two polyproteins, ORF1a and ORF1b. These polyproteins are further processed to generate the non-structural proteins (nsp). ORF1a is contributed to produce the nsp1-nsp11, while the rest of nsps (nsp12-nsp16) are originated from the ORF1b. Additionally, the viral structural proteins comprising surface (S), envelope (E), membrane (M), and nucleocapsid (N) proteins encoding by one third of genome at 3´ end. Viral proteins have been broadly considered as targets for antiviral therapies, but the problem arises when the selective pressure results to emergence of a new antiviral drug resistance lineage. Therefore, host coded factors and particularly, seem to be a better strategy MicroRNAs are a group of small non-coding RNAs, almost 19–24 base pairs in length. MiRNAs mediate their regulatory function through direct binding to the target transcript. Perfect pairing at the seed region (position 2 to 8 from 5’ end) has an important impact on the regulatory function of a miRNA. MiRNAs play a negative or positive role in viral-related processes in three ways: direct binding to the viral genome, binding to the viral transcripts, or binding to the host transcripts. Host miRNAs may promote viral RNA stability, replication, and infection or conversely, reinforced host antiviral responses against viruses. Since viruses are highly dependent on the host small RNAs (microRNAs) for their replication and propagation, we tried to predict top miRNAs involved in host-SARS-CoV-2 interface according to bioinfotmatics tools.

Methods: All human mature miRNA sequences acquired from miRBase database. MiRanda tool was used to predict the potential human miRNA binding sites on the SARS-CoV-2 genome. Additionally, the complete genome sequence of SARS-CoV-2 viruses isolated in the various geographical zones, including United states (MT322413.1), Spain (MT359865.1), France (MT470137.1), Japan (LC529905.1), South Africa (MT324062.1), India (MT415321.1), Brazil (MT350282.1), Australia

(MT007544.1), Korea (MT304475.1) and Kazakhstan (MT428554.1) were obtained from NCBI database.

Results: Among the 2654 human mature miRNAs, 444 miRNAs were identified with direct binding site on different positions along the coronavirus 2 reference genome. We focused on the interactions with perfect matching at the seed region and sorted out 160 miRNAs. Among them, there was 15 miRNAs with more than three binging sites and 12 miRNAs bound to the coronavirus 2 reference genome with a free energy (ΔG) less than -29 kCal/Mol. MiR-29 family (miR-29a, miR-29b, miR-29c) had the most binding sites (11) on the SARS-CoV-2 genome. miR-29a, miR-29b and miR-29c had 5, 2 and 4 sites respectively. six sites on ORF1ab, three sites on nucleocapside and two sites on spike sequences of the SARS-CoV-2 genome. In particular, we explored the binding pattern of miR-29 family among genome sequences released from 10 different geographical locations and found no mutation and 100% similarity.

Conclusion: MiR-29a directly bind to the 3'UTR of the HIV genome, increased the virus's transport to p-bodies and reduction of HIV replication. The inhibitory impact of miR-29a on HIV infection is mediated through binding to the accessory viral protein nef which is critical for viral persistence and release. Therefore, miR-29a has been considered as a potential therapy target for HIV eradication. Collectively, COVID-19 infection seems complicated and more experimental researches on the role of miR-29 family are needed to explore detailed molecular mechanisms of SARS-CoV-2 infection to clarify the similarities and differences between SARS-CoV-2 and other respiratory viruses.

Keywords: COVID-19; SARS-CoV-2; microRNA; microRNA-29 family

MicroRNAs 1234-3p and hsa-mir-382-5p Prevent Progression Of Proliferation and Tumor Spread by Targeting Oncogenic Genes in Glioma (Research Paper)

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Introduction: Glioma is the most common primary intracranial tumor, representing 81% of malignant brain tumors. Histologically, it shares specifications of normal glial cells and are generally named according to these similarities. However, whether gliomas cause from normal glial cells, glial or neural precursors, stem cells, or other cell types remains a topic of investigation. Tremendous progress in genomic, transcriptomic and epigenetic profiling has resulted in new concepts of classifying and treating gliomas. Therefore investigating the molecular targets of glioma is necessary for designing new therapeutic agents that will improve survival rate. MiRNAs are small noncoding RNAs (19–22 nucleotides) that post translationally regulate gene expression by causing mRNA degradation or inhibiting their translation through RNA interference. So this study purposes to evaluate the association between hsa-mir-1234-3p, hsa-mir-382-5p and glioma in pathways.

Methods: Specifications of miRNAs were obtained through mirbase, HMDD and miRdSNP. To identifying target genes, miRTarBase, MIRWALK2.0, TargetScan, DIANA Tools were used. Venn diagram used to identify common target genes between MiRNAs. GEPIA2 used to investigate gene expression in normal and brain tumor tissue. The signaling pathways for target genes which had high expression difference were observed from the DAVID database and the pathways associated with glioma were stored for interpretation. The network of genes was obtained from GENE MANIA.

Results: The result demonstrated that hsa-mir-1234-3p, hsa-mir-382-5p prevent cell growth and proliferation by activating PETEN which blocks AKT. In other side of the pathway mentioned microRNAs inhibit MTOR by blocking PI3KACT and AKT and effect on adhesion increasing by preventing cell survival and proliferation by blocking BRAF and RAS which active MEK1/2, ERK1/2 , RAF and BCL2 through phosphorylation and suppresses cancer.

Conclusion: hsa-mir-1234-3p and hsa-mir-382-5p act as tumor suppressor by inhibiting angiogenesis, proliferation and effect on adhesion increasing by preventing cell migration through inhibiting AKT BRAF,RAS and up regulating PETEN in PI3KAKT, neurotrophin ,ErbB and MAPK pathways.

Keywords: Glioma, Signaling pathways, MicroRNA, Oncogenic genes

MicroRNAS Role as Nuclear Factor Kappa B activator in Neurotrophin Pathway in Alzheimer's disease (Research Paper)

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Introduction: Alzheimer's disease (AD) is a neurodegenerative with insidious onset and slow progression that nowadays impress more than 40 million people worldwide which is predicted to exponentially increase in the coming decades. AD is defined by the accumulation of dense plaques of β-amyloid peptide (Aβ) and neurofibrillary tangles of hyper phosphorylated tau that cause impairment in memory, cognition, and daily activities. The nuclear factor-kappa β (NF-κβ) plays an important role in the progression of AD. Recently, microRNAs (miRNAs) have emerged as a novel class of gene regulatory elements with conserved roles in development and disease .so the purpose of our study is to investigate the relationship between microRNAs and NF-κβ in neurotrophin pathway.

Methods: The feature of microRNA was archived by using miRBase, HMDD and miRdSNP. Valid target genes and predict one were identified by miRTarBase, MIRWALK2.0, TargetScan and DIANA Tools. Venn diagram used to identify common target genes between MiRNAs .Gene expression in brain was obtained from The Human Protein Atlas. Finally, the pathway enrichment analysis was performed by the KEGG, David and ALZ path. GENEMANIA used to find gene network

Results: The result indicated that hsa-miR-1324, hsa-miR-185-5p, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-24-3p and hsa-miR-573 inhibit MAPK3 by blocking RAS which active ERK5 and MEK5 by phosphorylation. Mentioned microRNAs activate NF-κβ by inhibiting AKT, PDPK1 and PIK3CD in neurotrophin pathway and prevent Alzheimer development.

Conclusion: Factor nuclear factor-kappa B (NF-κβ) is a key regulator of innate immunity, in the major genetic and environmental risk factor in neurotrophin pathway of AD. Finally hsa-miR-1324, hsa-miR-185-5p, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-24-3p and hsa-miR-573 by acting as NF-κβ activator, prevent Alzheimer progression.

Keywords: Alzheimer's disease, Neurotrophin, MicroRNA, NF-κβ

MiRNAs role in the biology of pancreatic cancer (Research Paper)

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Introduction: Pancreatic cancer (PC) is the seventh most common malignancy which is one of the deadliest cancers in the world, as a consequence of late diagnosis, early metastasis and limited response to chemotherapy. The limited efficacy of current treatments necessitates the development of novel therapeutic strategies that are based on an understanding of the molecular mechanisms involved in pancreatic cancer progression. MicroRNAs (miRNAs) are non-coding small RNAs that regulate the expression of multiple proteins in the post-translation process which exhibit oncogenic or tumor suppressive activities by directly binding to their target messenger as advanced pancreatic therapies and have been identified to play a significant role in pancreatic cancer regulation. Profiling of deregulated miRNAs in pancreatic cancer can associate to diagnosis, indicate optimal treatment and predict response to therapy. Furthermore, understanding the main important genes in pancreatic cancer along with downstream pathways can identify possible miRNAs as therapeutic candidates.so this study aims to investigate miRNAs involvement in the biology of PC associated with their pathways.

Methods: MicroRNA specifications was accrued by using mirbase, HMDD and miRdSNP. The valid and predict genes obtained from miRTarBase, MIRWALK2.0, TargetScan and DIANA Tools. To identify common target genes between MiRNAs, Venn diagram used. GEPIA2 used to investigate gene expression in normal and pancreas tumor tissue. Finally, pathways archived from KEGG and David for genes with high expression difference. GENEMANIA was used to obtain gene network.

Results: The result dedicated that mir-202-3p ,mir-22-3p, mir-98-5p and mir-1237-3p by inhibiting Ras which actives Raf1, MEK, ERK through phosphorylation prevent proliferation of cancer cell and angiogenesis. IKK, NFkB were inhibited by blocking PI3K, which actives Ras. So MYC, BCL through inhibition cell survival, suppress cancer. Mir-199a-5p, and 3120d by inhibiting Ras, PI3K, IKK, NFkB through preventing cell cycle, prevent cancer development.

Conclusion: multiple signaling pathways are involved in the pathogenesis of PC, such as JNK, PI3K/AKT, nuclear factor kappaB (NF-κB) in which mir-202-3p mir-22-3p,mir-98-5p and mir-1237-3p by effecting on Ras, IKK, NFkB1, PI3K inhibit proliferation, angiogenesis and cell survival. Mentioned microRNAs by acting as tumor suppressor prevent cancer development and tumor spread by inhibiting proliferation of cancer cell, angiogenesis and sell survival

Keywords: Pancreatic cancer, Signaling pathways, MicroRNA, tumor suppressor

Modeling and Molecular dynamic simulations of a scorpion potent potassium channel blocker: aid in drug development (Research Paper)

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Introduction: Scorpion venom is an important source for biologically active components that can modulate the ion channels (K+, Na+, Cl-, Ca2+) of the human cells. This concept of scorpion-derived peptides could be used to develop new specific drugs. Potassium channels blockers(KTxs), one group of scorpion venom toxins, can be good candidate for treatment of different disease, ranging from asthma, diabetes, angina, cardiac ischemia and hypertension to chronic inflammation, autoimmune disease and cancers. Transcriptome analysis techniques revealed some peptides in the venom gland of Iranian Mesobuthus eupeus, including many toxins. One of them named meuK5_1 that submitted in data bank in certain accession number (KU253402).

Methods: Homology modeling was performed with the program MODELLER for calculation of the 3-D model of meuK5_1. To optimize the obtained homology models molecular dynamic simulation was applied. Molecular dynamic simulation was done with the help of NAMD 2.9 and a time step of 2 fs for 20 ns (10 million steps). CHARMM 27 was utilized to parameterize. VMD software was employed to visualize the trajectories and their analyses, to wit: RMSD and RMSF, radius of gyration and solvent accessible surface area (SASA). Functional similarity of peptides of the same family was used to explain the function of meuK5_1 in which the amino acid residues that could be involved in the potassium channel/toxin interactions was proposed.

Results: The cDNA sequence of meuK5_1 consists of 262 nucleotides that encodes for a precursor with 16AA signal peptide and 42AA mature peptide in length. Refined 3-D structure of meuK5-1 consists of a conserved CSα/β (cysteine-stabilized α-helical and β-sheet) in which a single α-helix connected to a double stranded β-sheet through three disulfide bonds. The connectivity pattern of disulfide bridges is: Cys15-Cys33, Cys19-Cys28, and Cys23-Cys40. functional analysis suggests a key role for residues Lys32 and Tyr41 of meuK5-1 as a “functional dyad” in the interaction and blockage of the potassium channels. According to the current view, Tyr41 interacts with a cluster of ion channel aromatic residues. Then, the side-chain of the Lys32 residue positions itself into the channel pore and interacts with selectivity filter of the channel and thus blocks it.

Conclusion: The information obtained here can be utilized to direct more exploration for better understanding of meuK5-1 to develop a potent pharmaceutical.

Keywords: scorpion toxins, Mesobuthus eupeus, drug development, modeling, molecular dynamic simulation

Modeling of streptokinase mutants and evaluation of their Intermolecular interaction with microplasmin (Research Paper)

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Introduction: Thrombosis of blood vessels in different organs especially in heart can lead to irreversible consequences if not acted in time. Streptokinase as one of the most important thrombolytic drugs may be engineered to be used repeatedly and safely for patients who suffer from such a dangerous disease.

Methods: Mutant streptokinase proteins, having cysteine residues in their structure, were modeled and docked with their counterpart in the active enzymatic complex and their intermolecular interaction was compared to the intact streptokinase.

Results: The results showed that the mutant protein containing cysteine at 263 and 319 sites increased 6.89% of buried surface area but on the other hand RMSD between alpha carbons from the lowest energy structure increased from 1.1 to 1.3

Conclusion: These results showed that these cysteine residues may confer more flexibility to streptokinase structure and increase the ability of the activator complex for higher activity. Experimental analysis is required to be carried out to demonstrate this primary results

Keywords: Mutant, streptokinase, docking , RMSD

Modulation of the expression of fibrotgenesis related long non-coding RNAs by endurance exercise in the hearts of rats with myocardial infarction (Research Paper)

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Introduction: Cardiovascular diseases (CVDs) are the first cause of death worldwide. Coronary artery diseases (CADs) including myocardial infarction (MI) account for about 40% of CVD-related deaths. Low physical activity is one of the important risk factors for CADs. Physical activity (PA) dramatically lowers the risk of CADs, including MI, by up to 50% . It has been shown that as a basic part of cardiac rehabilitation programs, exercise training reduces mortality and re-infarction and improves quality of life in patients suffering from CADs, especially MI and heart failure (HF). The previously assumed “junk DNA” encodes for a group of non-coding RNAs (ncRNAs) as a new layer of gene regulation. Non-coding RNAs are classified according to the length of the oligonucleotides into small (20-25 nt) (microRNA) and long (> 200 nt) (LncRNAs) ncRNAs. LncRNAs comprise about 70% of ncRNAs and their regulatory function is emerging in a wide range of genomic and cellular processes including chromatin remodeling, genomic imprinting and post/transcriptional regulation, cell differentiation and invasion. Given their abnormal expression in cardiac diseases, lncRNAs have been regarded as potential therapeutic targets for CVDs. Dysregulation of lncRNAs H19, myocardial infarction association transcript (MIAT), and growth arrest specific 5 (GAS5) has been previously reported in MI. H19 as a regulator of extracellular matrix (ECM) facilitates fibrotic procedures at early stages of cardiac remodeling after MI. MIAT has been introduced as a pro-fibrotic lncRNA in the pathogenesis of MI. MIAT expression increases in the peri-infarct area and activates cardiac fibrosis through the MIAT/miR-24/Furin axis. Inhibition of GAS5 in isoproterenol induced MI models reduced cardiomyocyte apoptosis and ameliorated subsequent cardiac fibrosis.

Methods: Left anterior descending (LAD) coronary artery ligation was used as the model for MI induction in male Wistar rats. Animals were randomly divided into 4 groups: Sham, Myocardial Infarction (MI), Sham + Exercise (EXE) and Myocardial Infarction + Exercise (MI + EXE). Each group consisted of 12 rats. Exercise training (Ex) was performed according to 5 days/week, 50 min/day at 16 m/min program for four weeks following a five-minute warm-up at 10 m/min. In the end, hemodynamic parameters and cardiac function indices were measured. Masson is trichrome staining performed assessment of fibrotic areas. Expression of genes was evaluated by real-time PCR.

Results: Masson's trichrome staining indicated that Ex significantly reduced the fibrotic area of the hearts exposed to MI ($P < 0.05$). Ex normalized ($P < 0.05$) the increased left ventricular systolic pressure (LVSP) and heart rate in the MI group ($P < 0.05$). Ex returned the reduction of -dp/dt max that had accomplished during MI ($P < 0.05$). The expression of H19 was significantly reduced ($P < 0.01$) in MI group in compare with sham. We observed that the reduced expression of H19 ($P < 0.01$) in MI rats returned to normal levels by Ex. Ex significantly ($P < 0.001$) reduced the expression of MIAT and increased the expression of GAS5 ($P < 0.01$), which had changed in the hearts of rats with MI.

Conclusion: The present study indicated the beneficial effect of Ex on the improvement of cardiac function and reduction of fibrosis in infarcted heart possibly through regulation of the expression of lncRNAs: H19, GAS5, and MIAT.

Keywords: long non-coding RNA, exercise, myocardial infarction, H19, MIAT, GAS5

Molecular and biochemical mechanisms of human iris color: A comprehensive review (Review)

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Introduction: Abstract Eye color is determined as a polymorphism and polygenic trait. Brown is the most common eye color in the world, accounting for about 79%, blue eye color for about 8–10%, hazel for 5%, and green for 2%. Rare-colored eyes include gray and red/ violet. Different factors are involved in determining eye color. The two most important factors are the iris pigment and the way light is scattered from the iris. Gene expression determines the iris pigmentation and how much melanin is present in the eye, which is the number of melanin subunits that identify eye color. The genes involved in the pigmentation of single-nucleotide polymorphism (SNP) have a significant role; and even some genes are included only in the eye color through SNP. MicroRNAs also affect melanocyte synthesis, which is usually affected by the downregulation of essential genes involved in pigmentation. In this study, we assess the biochemical pathways of melanin synthesis, and the role of each gene in this pathway also has been examined in the signaling pathway that stimulates melanin synthesis.

Methods: REFERENCES Ambrosio, A. L., Boyle, J. A., Aradi, A. E., Christian, K. A., & Di Pietro, S. M. (2016). TPC2 controls pigmentation by regulating melanosome pH and size. Proceedings of the National Academy of Sciences of the United States of America, 113(20), 5622–5627. https://doi.org/10.1073/pnas.1600108113 Aoki, H., Yamada, Y., Hara, A., & Kunisada, T. (2009). Two distinct types of mouse melanocyte: Differential signaling requirement for the maintenance of non-cutaneous and dermal versus epidermal melanocytes. Development, 136(15), 2511–2521. Caliebe, A., Harder, M., Schuett, R., Krawczak, M., Nebel, A., & von Wurmb-Schwark, N. (2016). The more the merrier? How a few SNPs predict pigmentation phenotypes in the Northern German population. European Journal of Human Genetics, 24(5), 739–747. https://doi.org/10.1038/ejhg.2015.167 Chao, Y. K., Schludi, V., Chen, C. C., Butz, E., Nguyen, O. N. P., Muller, M., … Grimm, C. (2017). TPC2 polymorphisms associated with a hair pigmentation phenotype in humans result in gain of channel function by independent mechanisms. Proceedings of the National Academy of Sciences of the United States of America, 114(41), E8595–e8602. https://doi.org/10.1073/pnas.1705739114 d'Ischia, M., Wakamatsu, K., Cicoira, F., Di Mauro, E., Garcia-Borron, J. C., Commo, S., … Meredith, P. (2015). Melanins and melanogenesis: From pigment cells to human health and technological applications. Pigment Cell & Melanoma Research, 28(5), 520–544. D'Mello, S. A., Finlay, G. J., Baguley, B. C., & Askarian-Amiri, M. E. (2016). Signaling pathways in melanogenesis. International Journal of Molecular Sciences, 17(7), 1144. https://doi.org/10.3390/ijms17071144 Dynoodt, P., Mestdagh, P., van Peer, G., Vandesompele, J., Goossens, K., Peelman, L. J., … van Gele, M. J. (2013).

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Results: In this study, has been assessed the number of genes found in various articles related to eye coloration. The expression of each of the genes examined in this study plays a role in the development of eye color. It affects the amount, size,

pH, or pathways that influence melanin synthesis. One of the features of the genes involved in pigmentation is the high number of SNPs that affect specific SNP populations. In some countries, these SNPs are also used in forensic cases to diagnose people

Conclusion: Studying pigmentation in human is very important because the genes involved in pigmentation cause various diseases. This study further discusses eye color. We have about 80 different eye colors around the world, all of which are caused by the levels of eumelanin and pheomelanin. Changes in the amount of eumelanin and pheomelanin are influenced by genes that affect the biochemical pathway, signaling, or cellular and molecular structure issues of the melanogenic mechanism. In this study, has been assessed the number of genes found in various articles related to eye coloration. The expression of each of the genes examined in this study plays a role in the development of eye color. It affects the amount, size, pH, or pathways that influence melanin synthesis. One of the features of the genes involved in pigmentation is the high number of SNPs that affect specific SNP populations. In some countries, these SNPs are also used in forensic cases to diagnose people. Some genes such as HERC2 or CYPs are not pigmentation genes just because of their effect on eye color through the SNP in these genes. miR also has a significant impact on pigmentation through the expression of genes involved in the production of melanin. miR can increase or decrease the amount of melanin, which changes the amount of melanin to alter the balance of eumelanin and pheomelanin and produce different eye colors. The purpose of this study is to provide complete information on eye color determination.

Keywords: eumelanin, iris color, melanin pathway, pheomelanin, pigmentation gene

Molecular and morphology conflict: a case study on two species of the genus Protracheoniscus (Isopoda; Oniscidea) (Research Paper)

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Introduction: Terrestrial isopods of the genus Protracheoniscus Verhoeff, 1917 include 62 species; some of them are among the first isopod species described. The genus has a large distribution range in the palearctic and oriental regions. While most of their type localities, others show a broad distributional range. Compiling morphological and molecular data help frequently researchers to define the accurate taxonomic name could truly assign to the individuals of a given species. The gene coding mitochondrial cytochrome c oxidase I (COI) has been commonly used for DNA barcoding and species identification in invertebrate in general and terrestrial isopods in particular. In this study, morphological features and molecular evidence were exploited for the first time to determine whether P.nogaicus and P.darevskii belong to the same species or deserve to be ranked as two valid species.

Methods: Genomic DNA was extracted from specimens preserved in 96% ethanol using the Qiagen method. The partial mitochondrial cytochrome c subunit I (COI) was amplified using the universal primers; HCO2198/LCO149. PCR products were sequenced using a dye-labelled di-deoxy terminator cycle sequencing with Big Dye V.3.1. The final alignment of 682bp of COI gene was aligned using Clustal X algorithm implemented in BioEdit. Phylogenetic tree was constructed using two probabilistic algorithms, Bayesian inference (BI) and Maximum Likelihood (ML) analyses. Nodal supports for ML analysis were estimated using 1000 non-parametric bootstrap (BP) replicates, and Bayesian posterior probabilities (BPP) were used to assess branch support of the BI tree.

Results: Specimens from Mahabad and Bostanabad identified to belong to P. darevskii, and were compared to P. nogaicus which we found no distinct difference discriminating them from each other. The BI and ML trees gave very similar topologies. In which P. darevskii did not hold a distinct position on its own instead was clustered closely to P.nogaicus from Russia.

Conclusion: It is obvious that molecular studies are dramatically re-shaping our understanding from the species evolution, biodiversity, and geographic pattern of intraspecific variations. Comparing the pairwise genetic distance indicated that the mean genetic divergence between P. darevskii and P. nogaicus confidentially placed within intraspecific divergence estimated in the terrestrial isopod species while it varies for other analyzed species of Protracheoniscus. All these findings proposed that P. darevskii cannot be a true species but instead a morphological variant of P. nogaicus. The present study, therefore, indicates that the two species

belonging most probably to the same species but adding specimens from type locality to the analysis is crucial for definite decision.

Keywords: Terrestrial Isopods, Molecular Marker, Morphology, Species Delimitation, Synonym

Molecular and phenotypical features of the Jalili syndrome: A systematic review (Review)

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Introduction: Jalili syndrome (JS) is a rare recessive syndrome that has been reported in all five continents. The first and the Most reported cases of this syndrome are in the Middle East. Patients with JS suffer from two main symptoms, amelogenesis imperfecta (AI) and cone-rod dystrophy (CRD). Nystagmus, photophobia, loss of vision, and tooth decay are the main reported complications in these patients. It has been reported JS patients have mutations in the CNNM4 gene, an mg2+ transporter in the cell. In the current systematic review, previous cases of Jalili syndrome and identified mutations in the CNNM4 gene have been discussed to get to a better understanding of the disease and possible Genotype-phenotype correlations.

Methods: The current systematic review was performed according to the PRISMA statement. Public medical databases including PubMed, Embase, ProQuest, and Cochrane were searched to find published articles. Studies that discussed cases of Jalili syndrome and/or reported its mutations were included in the study.

Results: A total of 3473 studies were identified in search of databases. Title and abstract of studies were evaluated and 2468 studies were excluded and 25 studies remained. The full text of remaining studies was evaluated and none were removed. To date, a total of 134 patients with Jalili syndrome have been identified. CRD and AI were both simultaneously reported in Jalili syndrome patients. Three other studies have discovered additional symptoms including mental retardation, situs inversus, keratoconus, and muscular overgrowth. There are three reported cases of this syndrome in Pakistan, India, and Gaza which lack molecular evaluation. All cases had mutations in the CNNM4 gene. The protein-protein network of the CNNM4 gene was also evaluated.

Conclusion: The previous cases of the JS were discussed in this article. Due to the limited number of studies, no phenotype-genotype correlation could be concluded. The proteins that are in functional correlation with CNNM4 are also

reported in patients with ocular disorders. So, further study on the protein network of the CNNM4 may give a better understanding of the molecular etiology of JS. The JS cases are mostly identified in the countries with higher fluoride concentration in their groundwater. The higher ground fluoride concentration may result in increased mutation level in individuals. Further studies are required to confirm this hypothesis.

Keywords: Jalili syndrome; CNNM4; Cone-rod dystrophy ; Amelogenesis imperfecta

Molecular detection of Trichomonas vaginalis and Toxoplasma gondii in Rattus norvegicus from Tehran province, Iran (Research Paper)

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Introduction: Rodents have become a threat to public health worldwide and they are reservoirs for transmission of zoonotic parasites. Given the large number presence of rodents throughout the city of Tehran, this study aims to assess the frequency of Trichomonas vaginalis and Toxoplasma gondii carried by commensal Rattus norvegicus wandering in Tehran, Iran.

Methods: The serological test was applied in order to detect effective antibodies against Trichomonas vaginalis using a commercial qualitative rat ELISA kit. The polymerase chain reaction was employed to detect the presence of Toxoplasma gondii in commensal Rattus norvegicus dispersed in Tehran.

Results: A total of 50 live Rattus norvegicus were captured and surveyed in order to determine their zoonotic parasites. Seroreactivity against Trichomonas vaginalis was detected in 6% (n = 3/50) of the Rattus norvegicus tested. Toxoplasma gondii DNA was detected in 16 out of 50 (32%) Rattus norvegicus.

Conclusion: The present study is the first research to have investigated the prevalence of Trichomonas vaginalis in the Rattus population, worldwide. The finding of our study indicates that the Rattus norvegicus population is a significant reservoir of Toxoplasma gondii infection for humans in Tehran. Information about zoonotic parasites carried by the Rattus norvegicus population in Tehran province is critical to developing suitable surveillance plans and intervention strategies.

Keywords: Trichomonas vaginalis; Toxoplasma gondii; Rattus norvegicus; Tehran

Molecular Detection Of Virulence Genes Involved In Cytolethal Distending Toxin (CDT) Production In Campylobacter jejuni And Campylobacter coli Isolated From Poultry Faeces (Research Paper)

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Introduction: Food-borne disease is an important problem worldwide that can be caused by the ingestion of public health bacteria, virus, fungi, and parasites, or toxins that have contaminated food(Abebe et al., 2020). Campylobacter jejuni and Campylobacter coli are the major food-borne pathogens that cause human bacterial gastroenteritis in both developed and developing countries(Zbrun et al., 2020). Every year, approximately 1% of the population in Europe is contaminated with Campylobacter(Epps et al., 2013). Many domestic animals, such as poultry are considered reservoirs for Campylobacter spp. (Khoshbakht et al., 2013). Campylobacter jejuni and Campylobacter coli are often related with the development of immunoreactive confusions. For example, these may lead to polyarthralgia, GuillainBarre, and Miller Fisher disorders, and eventually death(Casabonne et al., 2016). Several genes have been linked to Campylobacter virulence, but the most important are cytolethal distending toxin (cdt), which disrupts mucosal ¬barriers by causing host cell death (Barakat et al., 2020). Cytolethal distending toxin (cdt) in Campylobacter spp. is among the significant virulence factors of these bacteria in the intestine(Gharajalar et al., 2020).

Methods: To perform the study 182 fecal samples were collected from poultry . All samples were subjected for isolation of Campylobacter spp. using prêt KB method and the presumptive isolates authenticated by DNA sequencing of 16srRNA genes. Finally, Campylobacter isolates assessed for detection of Cytolethal distending toxin (cdt) gene.

Results: Sampling from the poultry faeces was conducted between March 2019 and August 2019 in behbahan city, khuzestan province, iran. The results obtained indicated that 39 strains of Campylobacter spp. were isolated. Among the 39 Campylobacter strains, including 30 Campylobacter jejuni and 9 Campylobacter coli, the prevalence of cdtA, cdtB, cdtC, virulence genes were 69.23% (27/39), 84.62% (33/39), 84.62% (33/39), respectively.

Conclusion: The research works on the virulence characteristics of potentially pathogenic bacteria in domestic animals and in foods containing animal origin are essential for the safety of the user. Although for assessing campylobacteriosis risk, heterogenic identification and virulence of genes of Campylobacter species isolated from the faeces samples of poultry are needed, so far it has not been done in the Khuzestan province. Different measures for the clarity of variable clinical type

associated with Campylobacter infection have been suggested and phenotypic characteristics associated with different Campylobacter species could be related to their genetic variation. So, the aim of this study is to evaluate the prevalence of virulence-associated genes(CDT genes) in Campylobacter jejuni and Campylobacter coli isolates from poultry faeces samples. One of the other common virulence genes is cdt, which relates to cytotoxin production. This toxin is composed of three components cdtA, cdtB, and cdtC. By interference with division and cell disparity in the intestinal crypts, it causes diarrhoea. The presence of each of the three subunits is required for total toxin activity. CdtA and cdtC are essential for connection to the host cell. CdtB is an active section that enters the cells, arrests the cell cycle in the G2/M stage, and leads to cell death. Our research results demonstrated that the prevalence rates of cdtA, cdtB, and cdtC genes were 69.23% , 84.62%, 84.62%, respectively. Our research showed that the prevalence of genes involved in toxin production is more compared to genes involved in adherence and invasion. The results of our study showed that over 80% of the Campylobacter isolates have genes interfering in toxin production (cdtB, cdtC), which signifies that most of the Campylobacter isolates have powerful pathogenic .

Keywords: Campylobacter, Virulence genes, Cytolethal distending toxin, Poultry, Molecular Detection

Molecular diagnosis in the cardiology is a tool for personalized medicine (Review)

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Introduction: Personalized medicine is an ancient science with new approaches. Personalized medicine aims to design strategies for prevention and medical care by considering the conditions of environmental diversity, genetic lifestyle, and molecular phenotype for the individual.

Methods: Using clinical genomics to select the appropriate treatment as well as predicting outcomes are the first uses of this approach. The new Metabolomics field is emerging as a conceptual measurement of all low molecular weight metabolites and molecules in a biological sample. Since the purpose of Metabolomics is to provide a profile of a wide range of metabolites and, of course, to cover biological processes and metabolite pathways. It can be used as a powerful and essential tool in the molecular process of personalized medicine.

Results: Since heart disease, like most illnesses, has a genetic background, in this new style of medicine, by using molecular characteristics of each person, treatment and a suitable lifestyle are provided for that person. By utilizing advanced molecular and cellular technologies, diseases are predicted and prevented in a timely manner. Personalized medicine strategies include: disease diagnosis in the early stages, determining the program and treatment strategy for each person, monitoring the treatment process, monitoring the recovery process after treatment. Whereas people's genetic is unique, so each person needs a specific lifestyle and treatment.

Conclusion: The findings showed that mutation in the process of heart development leads to heart disease. Some transcription factors, cellular binders or proteins in the signaling pathway which are involved in heart function, are likely to play a role in the development of heart disorders. Genomics includes the analysis of genetic data, especially the genome of organisms. The information in the genome causes hereditary traits (phenotypes). Genomics can evaluate genetic factors in the risk of heart disease before occurring and getting infected. We hope in the near future personalized medicine, with methods based on molecular cognition as a powerful tool, can determine the suitable drug, the appropriate dose, and the right patient. And by connecting between different fields of biology and medicine, it becomes a powerful tool in the prevention, diagnosis, and treatment of diseases.

Keywords: Personalized medicine, Metabolomics, cardiology, Genomics

Molecular docking study of lignanamides from Cannabis Sativa against P-glycoprotein (Research Paper)

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Introduction: P-glycoprotein (P-gp), which was first identified in cancer cells, is an ATP-dependent efflux transporter that expels a wide variety of cytotoxic compounds out of cells. This transporter can decrease the bioavailability of therapeutic drugs by preventing their sufficient intracellular accumulation. Over expression of P-gp in cancer cells lead to multidrug resistance (MDR) phenotype that is one of the main reasons for the failure of chemotherapy. Hence, P-gp inhibition is a favorable method to reverse MDR. In this study, the lignanamides from Cannabis sativa were docked against P-gp to recognize potential binding affinities of these phytochemicals.

Methods: To study the binding modes of ligands in drug-binding pocket of P-gp, the crystal structure of P-gp (PDB ID: 4Q9H) was retrieved from Protein Data Bank (PDB; http://www.RCSB.org). The lignanamides from Cannabis sativa including cannabisin A, B, C, D, E, F, G, M, N and grossamide were used as the ligands. Tariquidar and zosuquidar, two well-known P-gp inhibitors, were selected as the control ligands. To get ready the structures, adding hydrogens and energy minimizing were performed by Molegro Virtual Docker and Chimera 1.13. Docking calculations were done by using Autodock vina in PyRx 0.8 to determine the best pose of each of the ligands (the most negative binding affinity). Finally, LigPlot+ was used to analyze protein-ligand complexes based on the type of interactions (bonding and nonbonding). In addition, to analyze absorption, distribution, metabolism and excretion (ADME) properties, the canonical SMIIES of the ligands were submitted to swissADME.

Results: Our study demonstrates that the lignanamids interacted with important residues in drug-binding pocket of P-gp with acceptable binding affinity ranging from -8.9 to -10.2 kcal/mol. Among the ligands best binding affinities were related to cannabisin N and cannabisin M that both have been docked with P-gp with most negative binding affinity (-10.2 kcal/mol) compared to tariquidar and zosuquidar (binding affinity: -10.1 and -9.6 kcal/mol respectively). Based on ADME properties, grossamide, cannabisin F and cannabisin N obeyed ‘Rule of 5’ with 1 violation (MW>500) and consecuently are druglikeness.

Conclusion: These data suggest that cannabisin M and cannabisin N could be good drug candidates against P-gp. But more studies are needed in order to prove these results.

Keywords: P-glycoprotein, ABC transporter, Cannabis, Lignanamide, Molecular docking

Monoclonal antibody therapy in the treatment of asthmatic Rats (Research Paper)

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Introduction: Bevacizumab (Avastin) is a humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody for cancer therapy. This drug can reduce the level of VEGF and has been widely used to treat various cancers, and Lung diseases such as COPD. Therefore the aim of this study was consider the effects of Bevacizumab on receptor 2 (VEGFR2) and lung inflammation of ovalbumin-induced rat.

Methods: Twenty one male Wistar rats were randomly divided into three groups (n=7 in each): 1) control, 2) ovalbumin (OVA)-sensitized and 3) OVA-sensitized with Bevacizumab (OVA+Bmab). Two and three groups were sensitized with ovalbumin (OVA) and aluminum hydroxide at day 1, 8 and challenged with OVA at day 15 by atomization for 10 days (inhalation). After OVA sensitization the OVA+Bmab treated with Bevacizumab for 2 weeks. VEGFR2 was semiquantitatively analyzed in lungs by immunohistochemistry. The gene expression of IL-10 was measured by real time PCR.

Results: Ovalbumin exposure promoted the expression of VEGF and result in inflammatory factors overexertion ($p \leq 0.05$). However, rats in OVA+Bmab group showed significantly decrease in VEGFR2 and significantly increased in IL-10 ($p \leq 0.05$).

Conclusion: The results show that Bevacizumab efficiently diminishes bronchial inflammation via reduced expression of VEGFR2 and anti-inflammatory cytokine (IL-10). Regarding the effectiveness of Bevacizumab, it seems that these FDA approved drug Bevacizumab has potential therapeutic value for controlling asthma disease.

Keywords: Bevacizumab; Asthma; VEGF; IL-10

Move to immortality with the Cryonics technique (Review)

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Introduction: Introduction: Cryonics is derived from the Greek word Kryos meaning cold or freezing at low temperatures. Cryonics is a technique in the hope that the scientific practice of the future will one day resurrect legal dead people and bring them back to youth and health. This technique involves extracting blood and then cooling the corpses to a liquid nitrogen temperature, usually −196 ° C or −320.8 ° F or 77.1 Kelvin, in which the storage of a human or beheaded body is stopped from decay. It is said that the person kept in such a state is a frozen patient because the creators of this technique do not necessarily consider the frozen person dead.

Methods: Materials and Methods: In this review study, searches were conducted in the electronic and scientific databases of PubMed, Medline, Google scholar, Scopus and ISI, and valid articles related to the subject were searched using the keywords Cryonics and Freezing.

Results: Results: Certainly, with the progress of this technique, a new step can be taken in the discussion of immortality. Also, research in this area could make it possible to preserve some specimens of endangered species such as animals and plants.

Conclusion: Conclusion: Low temperature slows down biological time and effectively stops at liquid nitrogen temperature. For humans, freezing is a means of achieving a biologically stable state that is essentially reversible. Preservation of cells, tissues, and organs by Cryonics suspension can transfer a mortal patient to future medical technology and immortalize the individual.

Keywords: Keywords: Cryonics, Freezing, Immortality, Liquid nitrogen

mRNA-based SARS-CoV-2 Vaccine (Review)

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Introduction: The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a deadly respiratory pathogen found in china at first and around the world in a short time. Due to the negative impact that this virus has imposed on the world economy and additionally, the high incidence and mortality rate of this virus, like other emerging diseases, the need for an effective and safe vaccine is very much felt. Therefore, many institutions and health investors in a competitive environment have focused their efforts on finding a vaccine that can provide potential and sustainable immunity in the absence of adverse effects against the virus. In this way, mRNAs as antigen encoding nucleic acids synthesized for immunogenic purposes called attention of researchers for investment. The aim of this study is to provide an overview of the initial data released from the latest findings of the new coronavirus mRNA-1273 vaccine

Methods: To write this article, four scientific databases including: PubMed, Science direct, Scopus and Google scholar plus Google search engine were reviewed by a systematic search for all available data both in the form of published articles and in the form of scientific texts and news. The search keywords were: “SARS-CoV-2”, “Vaccine” and “mRNA-1273” and the time ranged from December 2019 to September 2020.

Results: MRNA-1273 is an RNA molecule which is collaboratively developed by the Cambridge, Massachusetts-based biotechnology company Moderna, Inc., and the National Institute of Allergy and Infectious Diseases (NIAID), synthetized with the ability to encode the prefusion stabilized spike protein as an immunogenic antigen which is packaged in lipid nanoparticles and delivered into the cells and to translate into surface proteins and present to the antigen-presenting cells, which ultimately produces a strong response of neutralizing antibodies and induces cellular immunity by stimulating T-helper cells and cytotoxic cells immunity which seems to play a more effective role than antibodies in clearing the virus from the body. The vaccine has also been able to reduce viral titers in the respiratory tract of studied models. In terms of side effects, this vaccine has been reported to have no pathological or other serious cellular effects. Phase 1 and 2 of clinical trials which began in March and May 2020, showed favorable results that encouraged researchers to begin further studies in the third phase of clinical trials. The vaccine is currently in phase three of its confirmation trials and it is hoped that further tests will yield promising results.

Conclusion: Developing mRNA-based vaccines as non-infectious and safe, well tolerable as well as rapid in production vaccines worth to be considered for infectious diseases such as: coronavirus disease-19 (COVID-19). By reviewing

initial data, we conclude that mRNA-1273 could provide an acceptable level of humoral antiviral immunity to SARS-CoV-2 as well as safety for vaccine recipients which can be considered as one of the potential vaccines in this case. Of course, the final approval of this vaccine for use in all human cases requires the completion of clinical trials, and therefore the effectiveness and safety of this vaccine cannot be predicted without considering other testing steps.

Keywords: mRNA-1273, Vaccine, SARS-CoV-2

Msc therapy, a new attitude in covid-19 treatment (Review)

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Introduction: In 1991, Arnold L. Kaplan named mesenchymal cells which are produced during embryonic development as mesenchymal stem cells (MSCs). These cells, which originate from the bone marrow, fat, umbilical cord, placenta, etc., are feed from many sources. They are multipotent and can differentiate into a variety of cell types. MSC therapy has been used effectively to treat acute respiratory distress syndrome (ARDS) caused by the H7N9 influenza. Given the similarity of H7N9-induced ARDS to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)-induced ARDS, it is the most promising treatment option.

Methods: Article selection were conducted through advanced search in science direct, Pubmed database and without time limit, using two keywords derived from MeSH (Covid-19 and Cell therapy) and limiting the search to keywords in the abstract. From the 68 available articles (25 original articles and 43 existing non-original articles), based on the content of the abstracts, 10 original articles and 26 non-original articles related to MSC therapy were selected. The articles were studied and key points of each were identified.

Results: MSCs do not have Angiotensin-Converting Enzyme 2 (ACE2) receptors, which makes them safe against Corona Virus disease 2019)Covid-19(. Because the key to treating Covid-19 infection lies in the management of the cytokine storm in the lungs, they secrete leukemia inhibitory factor (LIF), which is a factor in fighting the Covid-19 cytokine storm. Due to their main mechanism, MSCs work well through their immunomodulatory and anti-inflammatory properties. MSCs isolated from most tissues typically express CD105, CD73, and CD90 and lack the expression of bleeding markers such as CD45, CD34, CD14 or CD11b, CD79a or CD19, and HLA-DR. Their interventions include improving lung function and pulmonary fibrosis, rearranging the functions of immune cell subsets, regulating inflammatory cytokines, inhibiting the abnormal activation of T lymphocytes and macrophages, and differentiating into T-regulatory subsets (Treg) and anti-inflammatory macrophages. Their low immunity due to the lack of HLA-Class II antigen makes them an ideal candidate for allogeneic transplantation. Another advantage is that they have a high reproduction rate. They are easier to manipulate

and store and cost less than monoclonal antibody therapy. The cells are safe and intravenous injection is less likely to cause embolism. However, aspects of MSCs production that can affect cell function, such as place of production, donor age, cell source (umbilical cord, bone marrow, adipose tissue, etc.) and in-vitro expansion rate, may be sources of heterogeneity. Extensive research over the past decade has shown that MSCs exert most of their function through soluble mediators and extracellular vesicles (EVs). EVs have several advantages over cell therapy, including lower risk of tumorigenic effects, lower susceptibility to damage with hostile disease microenvironment, and the possibility of long-term storage. MSC-derived exosomes (MSCs-Ex) are also key therapeutic effects of these cells, which regenerate tissue and can be a viable alternative to cell therapy. MSCs-Exs can secrete a wide range of cellular proteins that support immune responses and neutralization of antibody titers. These exosomes are considered important because of their multifaceted role, from therapies to drug delivery and diagnosis. However, despite these benefits, only a handful of clinical trials are available to use these nano cells. One of the most important challenges that needs to be addressed is maintaining their stability and performance over a period of time.

Conclusion: In some stages of Covid-19, where cytokine storm is responsible for pathogenicity and inflammation, MSCs are more effective and less harmful candidates than other treatments and can be used as an effective treatment strategy to combat inflammation and destruction of lung tissue. However, more randomized clinical trials are needed for widespread use.

Keywords: COVID-19, Cytokine storm, Mesenchymal stem cells

Music therapy for reducing elderly depression who are kept in nursing homes (Review)

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Introduction: The elderly usually get depressed because of relocation of life, being away from their children and relatives and also lack of pleasure and enough attention and this depression increase the risk of death from other disease that the elderly have. On the other hand depend on recent world research, music decrease undesirable feelings like anger, sadness and stress which are symptoms of depression. Excitement, mood, vision and emotion are influenced by the music therapy process. Therefore studying the impact of music on the elderly can present a solution that prevent the progress of depression.

Methods: Since most elderly are kept in nursing homes have depression because of being away from their children and relocation of life, this research investigates the effect of music on depression of these kind of elderly. In this case study, first the two important parameters "heart beat" and "blood pressure" which are affected directly by depression measured. All cases in this study have a high level of consciousness and they don`t have Alzheimer.In the second step all of them listen to a Mozart music which is played by a headphone for them and after that for the second time the "blood pressure" and "heart beat" measured. The duration of music is the same for all of them. Then according to recorded data, we plot a graph for the two variables, "blood pressure" and "heart beat", and then analyse the data.

Results: The study was conducted on 14 elderly (6 women and 7 men). After comparing "heart beat" and "blood pressure" before and after listening to music, the increase in both of them was clear. 93% of elderly show the increase in their "heart beat" and "blood pressure" and only one of the elderly has a decrease in these two parameters. After 10 or 15 minutes, the "heart beat" and "blood pressure" again return to pre-test mode but all of the elderly declare that they feel happier than before the test.

Conclusion: Music affects the depressed human mind and it also harmonizes the mind and body and improve the quality of life. Listening to music causes the neurotransmitter Serotonin and Dopamine to be release more quickly , these two neurotransmitter have a huge impact on reducing depression. Also recent study about depression show that depression may rise because of low blood pressure and also with the decrease in the severity of the blood supply to the heart , the severity of depression increase . The rhythm of music also increase Serotonin , a neurotransmitter which decrease over years. This neurotransmitter continues to transmit nerve pulses and maintain happiness. Lack of Serotonin is one of the factors of depression. Serotonin increase the heart beat and blood pressure and by releasing of Histamine. Music also release Dopamine, neurotransmitter that affect nucleus accumbens. This area is the center of pleasure and regard and play a role in addiction. Dopamine also increase the blood pressure and it`s an cardiac

stimulator which increase cardiac output and contractile power with a positive chronotropic and inotropic effect on the myocardium. An important point is that too much increase in blood pressure is dangerous for elderly but Serotonin can decrease the danger of heart diseases . Since we are increase of blood pressure and heart beat after listening to music and the affects of the Serotonin and Dopamine on this increase , we can declare that music can cure depression to some extent. Play ,music for some hours in nursing homes for a while can improve depression and make elderly happier and feel better. Music have a huge effect on human body and recognizing these effects can help us to find some ways for treating some diseases , like depression that is an important problem for all people specially elderly people. At the end thanks to all the elderly and those who help us.

Keywords: Music therapy, Depression, Elderly , Blood pressure, Heart beat

Nanotechnology-based delivery of CRISPR/Cas9 system for genome editing (Review)

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Introduction: Gene therapy as a promising solution to treat a wide variety of diseases has attracted a great attention. The advent of endonuclease-based genome editing techniques such as Meganucleases (MNs), Zinc-finger nucleases (ZFNs), Transcription Activator-Like Effector Nucleases (TALENs) and CRISPR (clustered regularly interspaced short palindromic repeats) has revolutionized biotechnology and gene therapy [1]. The effective CRISPR system with its advantages such as power, high accuracy, high specificity, high sensitivity, low cost, simplicity and multiplexity has become a popular approach in molecular biology research with various purposes such as diagnosis and treatment, among the genome editing techniques [2, 3]. CRISPR system has two classes, class I includes type I, III and IV systems and class II includes type II, IV and VI systems. The CRISPR system consists of an endonuclease called "Cas" and a guide RNA sequence "gRNA" to identify and bind to the target site [4]. This genome editing system has a broad range of applications including imaging, screening, base editing, gene targeting, RNA editing and more [5]. However, the delivery of its elements into the target cells and subsequently the target genomic area is an important and determining factor in the success of the CRISPR genome editing system. CRISPR systems can be delivered in three formats including Cas9/sgRNA-Plasmid, Cas9/sgRNA-mRNA and Cas9/sgRNA-RNP into target cells for genome editing. Types of delivery methods including physical delivery methods (electroporation, microinjection and hydrodynamic injection) and viral delivery methods (adenovirus, lentivirus and adeno-associated viruses) are commonly used to deliver gene constructs. Overall, physical delivery methods, despite all their advantages, face challenges such as damage to cells, need for special equipment, high cost, cellular totoxicity, and so on. Despite their advantages and high efficiency, viral delivery methods also face disadvantages such as triggering an immune response, the risk of being integrated into the host genome and so on. Recently, different groups using nanomaterial-based delivery systems have successfully delivered CRISPR system components into target cells and carried out desired genomic operations. In general, delivery systems based on nanotechnology

have advantages such as easy synthesis, high efficiency, high load capacity, high specificity, applicability in vivo, low cost, suitable size etc [6, 7].

Methods: In writing this review article, we searched in various databases such as google scholar for keywords related to CRISPR and delivery methods, and selected the most suitable papers.

Results: Sun et al. were the first to be able to transfer the components of the CRISPR system into desired cells using a nanotechnology-based delivery system (DNA nanoclew). First, the DNA nanoclew was synthesized using the Roling Circle Amplification (RCA) method and then Cas9/sgRNA was loaded on it. Finally, they coated the DNA nanoclew-Cas9/sgRNA complex using polyethyleneimine (PEI) [8]. Mout et al. using arginine-functionalized gold nanoparticles were able to successfully deliver the Cas9/sgRNA ribonucleoprotein complex into target cells with 90% efficiency. Finally, by evaluating the efficiency of indel generation by this system, it was found that the efficiency of this system in indel generation in AAVS1 and PTEN genes in HeLa cells was 29 and 30%, respectively, and in PTEN gene in the HEK-293T and Raw 264.7 cells, the efficiency was 23 was 28%, respectively [9]. Ming et al. successfully introduced gene-modifying proteins, including Cre recombinase and Cas9/sgRNA, into human cells and rat brain, using bioreductible lipid nanoparticles. They synthesized 12 bioreducible lipids by adding primary or secondary amine groups and acrylate. It was observed that the negatively charged Cas9/sgRNA complex is capable of forming complex with bioreducible lipids for effective gene editing. The EGFP gene in HEK cells was selected as the target gene to evaluate the delivery efficiency of Cas9/sgRNA complex by bioreducible lipids. It was found that the established system leads to cleavage of the EGFP gene and induces the NHEJ repair system in the EGFP gene and ultimately leads to loss of cell fluorescence [10].

Conclusion: Nanotechnology-based delivery systems for the delivery of CRISPR system components can be considered as suitable alternatives to traditional delivery systems due to their advantages.

Keywords: CRISPR, Delivery, Gene editing, Nanomaterial

Necessity of cervical cancer screening in middle and low income countries (Research Paper)

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Introduction: : In low and middle income countries, cervical cancer is considered one of the common cause of cancer related- death in women. Even though cervical cancer has been controlled by cytology-based screening in developed countries, unfortunately the majority of women who develop cervical cancer live in societies with no or poor access to regular screening.

Methods: Method: All cases of cervical neoplastic lesions including Low grade squamous intraepithelial lesion(LSIL), High grade squamous intraepithelial lesion(HSIL), Insitu squamous cell carcinoma, insitu adenocarcinoma, Invasive squamous cell carcinoma(SSC) and invasive adenocarcinoma were retrieved from file of pathology department of university affiliated Alzahra hospital(Tabriz-Iran) from April 2016 to April 2018 to achieve of relative incidence of preinvasive and invasive cervical neoplastic lesions. Repeated surgical specimens from one patient were excluded.

Results: Result: A total number of 43 cases of cervical preinvasive and invasive neoplasia lesions were found in the study period, that can be prevented by using screening.

Conclusion: : Based on the results of this study, it can be concluded that, nowadays cervical cancer is considered truly a curable cancer if diagnosed in preinvasive or very early stages of invasive. We strongly recommend that national appropriate screening program in association with social education about HPV infection should be start in Iran.

Keywords: Key word: cervicalcancer, screening, middle income country

Neonatal Obstetric Syndrome (Review)

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Introduction: Methadone maintenance therapy is a standard treatment for the management of pregnant women with opioid-dependent. This treatment enhanced neonatal situation and decreased maternal mortality and morbidity. However, methadone can cause neonatal abstinence syndrome (NAS) which is characterized by respiratory distress and hyperirritability of the central nervous system. The incidence of NAS in infants exposed to methadone varies between 13% to 94%. In this paper, we aimed to investigate the relationship between maternal methadone dose and NAS.

Methods: We searched the keywords " Neonatal abstinence syndrome " AND "Maternal methadone dose" between 2015 and 2019 in PubMed, EMBASE and Google Scholar databases with no language restrictions. We included case-control, cohort and clinical trial studies. We found 27 articles that only 5 of them were related to our subject.

Results: According to the articles, increase maternal methadone dosage has a significant relation with the incidence of NAS. Each 5.5 mg increase in maternal methadone dosage has a direct relationship with 1 additional day of NAS treatment for the infant ($P < .001$; 95% CI, 0.112-0.255). Also, high maternal methadone dose increases the risk of preterm born, smaller symmetrically and the need for treatment for NAS.

Conclusion: The results of the studies show that maternal methadone dose is a significant risk factor for the expansion of NAS. So, it is very important to manage and predict the risk classification of NAS for infants of opioid-dependent mothers. Also, there is a need to investigate more suspicious of the potential effects of new methods towards the usage of higher methadone dose during pregnancy.

Keywords: Neonatal abstinence syndrome, Maternal methadone dose, Infant.

Neurological disorders concomitant with CML in patients taking Imatinib (Review)

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Introduction: Neurogenetics is a combination of genetic, neurology, psychology, and psychiatry which contributes to our complete understanding of differences in each individual. Neurogenetics communicates between genetic variants and individual differences in brain characteristics. Despite the advances in this field, there are still three challenges ahead, including: conducting research on individual variables with small effects, absence of detailed mechanisms and need to translate findings toward greater clinical relevance. The behavioral neurogenetics is a multi-stage study, which involves genetic factors, brain structure and function, neurobehavioral processes and environmental influences. Genetic conditions cause neurogenic disorders in children include fragile X, Turner, Klinefelter syndrome and etc. Imatinib is an oral tyrosine kinase inhibitor which impedes ABL and the BCR-ABL1 fusion protein in chronic myeloid leukemia (CML), c-KIT and the platelet-derived growth factor receptor (PDGFR) in gastrointestinal cancers (GIST). This drug causes hematologic response in 95% and major cytogenetic response in 60% of CML patients.

Methods: Central Nervous System Blast Crisis in Chronic Myeloid Leukemia on Imatinib Mesylate Therapy: Report of Two Cases. CNS blast crisis of chronic myelogenous leukemia in a patient with a major cytogenetic response in bone marrow associated with low levels of imatinib mesylate and its N-desmethylated metabolite in cerebral spinal fluid. Isolated Central Nervous System Relapse in Lymphoid Blast Crisis Chronic Myeloid Leukemia and Acute Lymphoblastic Leukemia in Patients on Imatinib Therapy. An Unusual Presentation of Chronic Myelogenous Leukemia: A Review of Isolated Central Nervous System Relapse. Chronic myelogenous leukemia presenting with central nervous system infiltration, successfully treated with central nervous system-directed chemotherapy followed by allogeneic stem cell transplantation. Prophylaxis of central nervous system leukemia: a case of chronic myeloid leukemia with lymphoid blast crisis treated with imatinib mesylate. pubmed

Results: New studies have been shown that due to the presence of efflux transporters (such as ABCB1 and ABCG2) in blood-brain barrier, the activity of these transporters can be effective in responding to imatinib. So presence of non-functional variants in these transporters cause accumulation of blast crisis cells in central nervous system (CNS) addition to imatinib effects on the CNS of adult and fetal, it also affects their peripheral nervous system (PNS).

Conclusion: There are still contradictory results about the neurological effects of imatinib on CNS and PNS. So, further studies are needed to solve these discrepancies and improve the treatment of CML patients with concurrent CNS disorders.

Keywords: "Neurogenetics" "Imatinib" "chronic myeloid leukemia"

New Beneficial Effects of Metformin on Melanoma Cancer Therapy In vivo and In vitro (Review)

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Introduction: Melanoma is one of the most aggressive and treatment-resistant human cancer. Melanoma is the most dangerous form of skin cancer these cancerous growths develop when unrepaired DNA damage to skin cells triggers mutations in which lead the skin cells to multiply rapidly and form malignant tumors (Patel, 2011). Dacarbazine is one a not typical alkylation agent that generally considered the most active agent for remedying malignant melanoma (Crosby et al, 2000). Melanoma is known for its notorious resistance to chemotherapy, a major obstacle to successful treatment. Diabetes mellitus was first investigated as a risk factor for cancer death at the beginning of this century (El-Arabey, 2017). The association between cancer and diabetes has been a motivation for us to look for prevention strategies that can affect both diseases and reduce their overlapping load. Metformin (1,1-dimethylbiguanide hydrochloride) is used as first line therapy for diabetic mellitus type 2. The in vitro and in vivo anti-melanoma effect of metformin was investigated using B16F10 mouse melanoma cancer cell line.

Methods: Melanoma cell line B16F10 was obtained from Applied Physiology Research Center, Isfahan University of Medical Sciences. In order to achieve 80% confluence on the culture plate, 5×105 cells were plated in DMEM (10% fetal bovine serum and 1% penicillin/streptomycin) at 〖37〗^° C in a humidified atmosphere with 5% 〖CO〗_2 and rested for 48 h. The cells were incubated in 96 well flat-bottom plates (104 cell/well) for cell viability and 6 well plate (5×105 cells/well) for flow cytometric analysis. The cells were treated with dacarbazine (group 2), metformin (group 3) and combination therapy (group 4). Group 1 didn't have any treat as a control. For in vivo experiment the mice were kept in individual cage. B16F10 were collected from cell cultures and subcutaneously implanted (3×105) in side region of mice. Seven day after incubation animals were administered metformin in drinking water (600 mg/kg) and dacarbazine intravenous injection (250 µg/kg) daily as in vitro grouping.

Results: According to our result cell viability, which was determined at various time intervals (24 and 48 h) and in the presence IC50 concentrations of the chemotherapy drug (0.7 mM), was reduced by ~50% following 24 h measured in ELISA reader at 570 nm ($p<0.001$). Our result showed the crucial role of cancer stem cell biomarkers activation as hallmarks of cancer. High levels of CD44 were detected in all samples (around 99%) that conclude that in malignant melanoma cells, a high level expression of CD44 is associated with increased metastatic risk. This study demonstrates inhibitory effect of metformin alone and combination therapy with chemotherapeutic drug, dacarbazine, on CD44 CSCs. Also administration of metformin led to a significant reduction in tumor size compared to the group treated with dacarbazine alone. Differences between study groups were

analyzed by an oneway analysis of variance (ANOVA) with a post-hoc method (SPSS 16.00).

Conclusion: These results provided that the drug combination induced significantly more apoptosis than when each drug is used individually. In addition metformin showed to target cancer stem cell and reduced CD44 expression (Breza & Magro, 2005). These data suggest metformin potential for counteracting and preventing melanoma resistance to chemotherapy. This is a very encouraging result with regard to the possibility of metformin becoming a new tool for melanoma research and treatment. According to the results of this study, metformin can be a good complementary drug to cancer chemotherapy. We believe that Metformin co-treatment with chemotherapy may prevent melanoma resistance and improve long-term survival.

Keywords: Melanoma- cancer stem cell- combination therapy

New insights into liver disease diagnosis (Review)

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Introduction: Non-coding RNAs are defined as functional RNA molecules that are not translated into proteins. They are involved in regulating of gene expression at the levels of transcription, RNA processing, translation, and protection of genomes from foreign nucleic acids. MicroRNAs are small, non-coding RNAs with a significant role in epigenetic modification that can regulate gene expression in various processes such as development, proliferation, cell signalling, and apoptosis at the post-transcriptional levels. Additionally, miRNAs expression profiles can function as biomarkers of various diseases. microRNA-122 (miR-122) the most frequent microRNA in liver is known as a central regulator of gene networks and pathways in hepatocytes, plays a crucial role in different aspects of hepatic function and in the progress of liver diseases. According to the importance of epigenetics changes in gene expressions during development and differentiation of the various cell types in an organism, in this review, we summarize the current advanced research in epigenetic regulation of miR-122 expression, miR-122 gene targets, and regulatory role of miRNAs in liver physiology and diseases.

Methods: This review involves available literatures about Epigenetic modification roles through specific miRNA (miR-122) in liver diseases such as Hepatocellular carcinoma (HCC), hepatitis C virus (HCV), hepatitis B virus (HBV), Fatty Liver Diseases (ALD/ NAFLD/NASH), Fibrosis, Auto-immune liver disease and liver Iron Homeostasis. Several databases, including PubMed, Web of Science, Science Direct, Springer Link, Wiley Online Library, and Google Scholar databases were searched using a list of suitable keywords obtained from the MeSH to find, collect and classify all relevant data published from January 2000 to March 2020. The number of records identified was 285 and the number of full-length studies included in final analysis was 120.

Results: miR-122 expression is directed by liver-enriched transcription factors (LETFs), such as hepatocyte nuclear factors (HNFs). In most cases, miR-122 can bind with the 3′ un-translated region (UTR) of target mRNAs and mediate repression or induction of the translation of the targets. In hepatocellular carcinoma (HCC) the miR-122 levels are frequently reduced compared with normal liver cells and miR-122 can reduce tumorigenic properties of HCC by targeting several genes involved in tumorigenesis, including ADAM10, Igf1R, SRF, cyclin G1 and ADAM17. While the expression of miR-122 in patients with HBV infection could be significantly decreased, miR-122 is required for HCV replication and mediates this regulation by direct interactions with two binding sites in the 5′UTR of HCV RNA. miR-122 also plays a crucial role in the regulation of cholesterol and fatty acid metabolism in the adult liver. Therefore, a role for it can be considered in fatty liver diseases. In fatty liver disorders, furthermore, mi-RNA-122 is involved in NASH

development, such as fatty acid synthase (FAS), and there is a significant increase in the level of mi-RNA-122 in patients with NAFLD and ALD. In hepatic fibrosis, miR-122 is downregulated in activated HSCs and targeting prolyl 4-hydroxylase via miR-122 led to decrease collagen maturation and ECM-production. Therefore, miR-122 along with other microRNAs may potentially serve as a biomarker for diagnosis fibrosis in liver diseases. Autoimmune liver diseases (AIH) is correlated with altered in miRNA expression and it is demonstrated that circulating of miR-122 were significantly elevated in patients. Moreover, miR-122 is involved in controlling systemic iron homeostasis and inhibition of miR-122 caused systemic iron deficiency.

Conclusion: In this systematic review, we have discussed the role of miR-122, the most abundant hepatic miRNA, in liver injuries. Due to the roles of miR-122 in hepatic functions and liver injuries, it can be considered as a sensitive biomarker for liver injuries. Moreover, miR-122 appears to be a promising candidate for effective therapeutic approaches against tumour and infectious diseases of liver. miR-122 may provide a novel strategy to slow down liver disease progression in the future.

Keywords: Epigenetic modification, microRNA, miR-122, Liver diseases, Diagnosis/ Prognosis.

New insights into relationship between orexin and diabetes mellitus (Review)

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Introduction: Diabetes mellitus (DM) is one of the largest epidemics the world has faced, both in developed and developing nations. DM may be classified into type 1 (T1D) and type 2 (T2D). T1D results from an absolute deficiency of insulin due to autoimmune destruction of pancreatic b cells, while T2D is defined by impaired insulin secretion and increased insulin resistance. Orexins A and B are hypothalamic neuropeptides involved in regulating feeding behavior, sleep-wakefulness rhythm, and neuroendocrine homeostasis. Orexin-producing neurons are located in the lateral hypothalamic area (LHA), perifornical area (PF), and posterior hypothalamus. The orexin actions are mediated by two G-protein-coupled receptors, orexin-1 receptor (OX1R) and orexin-2 receptor (OX2R) differentially distributed in the brain. Within the hypothalamus, OX1R mRNA is most abundant in the ventromedial hypothalamic nucleus (VMH), whereas OX2R is highly expressed in the tuberomammillary nucleus, paraventricular nucleus, arcuate nucleus (ARC), and LHA including PF. Orexin neurons can directly sense the nutritional status by responding to peripheral metabolic signals, such as glucose, leptin, and ghrelin. The expression of prepro-orexin mRNA is enhanced when blood glucose levels are low, and vice versa. On the other hand, orexin deficiency causes narcolepsy in humans, accompanied by an increased risk of obesity and type 2 diabetes. Therefore, considering the critical role of orexin in regulating blood sugar and its effects on diabetes, an attempt has been made to review this peptide hormone and its role in diabetes mellitus.

Methods: Orexin is involved in pancreatic hormone secretion. Therefore, It may be a modulator of insulin. Immunostaining of the human pancreas has shown that about two-thirds of insulin-immunopositive cells are contemporaneously positive for orexin. Peripheral orexin may originate from hypothalamus cells traveling through the blood-brain barrier or maybe produced peripherally by cells like the enterochromaffin cells of the intestines and pancreatic islet cells. The possible association of orexin with insulin resistance in type 2 diabetes mellitus (T2DM) has rarely been studied. Therefore, we attained to investigate the association between serum orexin concentrations and insulin resistance in type 2 diabetes mellitus.

Results: The previous studies found that Orexin-A (OXA) inhibits insulin secretion and stimulates glucagon secretion. In turn, others demonstrated that OXA exerts insulin secretion in vivo and in vitro; also, OXA lowered blood glucose level in mice with experimentally induced diabetes. An animal study showed that orexin receptor agonist protects against diet-induced obesity and the development of type 2 diabetes, whereas orexin-deficient mice were insulin-resistant. This evidence suggests that orexin signaling plays an important role in the development of high-fat-diet-induced insulin resistance and type 2 diabetes mellitus.

Conclusion: According to animal experiments, orexin has been shown to reduce blood glucose by stimulating insulin secretion from beta cells and reducing glucagon secretion, as well as a delayed but sustained increase in leptin levels. Orexin has also been shown to improve glucose intolerance through a direct effect on target organs such as adipose tissue in model mice. Therefore, changes in orexin secretion can affect blood sugar metabolism and directly or indirectly play a role in the development of diabetes mellitus. However, this issue needs further research in the future.

Keywords: Orexin, Diabetes mellitus, Insulin

Non Invasive diagnosis of Hemolytic disease of fetus and newborn by cffDNA (Review)

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Introduction: The most common cause of HDFN (Hemolytic Disease of the Fetus and Newborn) is Rh incompatibility between mother and fetus. The result of the incompatibility in the mother's body is the creation of allo-antibodies which can pass through the placenta and lead to lysis of embryo's red blood cells. HDFN may cause anemia, jaundice, hepatosplenomegaly, Kernicterus, encephalopathy and also abortion. Conventional methods including cordocentesis and amniocentesis, which are used to detect HDFN, are invasive and may lead to abortion, so the importance of NIPT (Non-Invasive Prenatal Testing) is revealed as this methodology does not have the risks of earlier methods and has high accuracy and sensitivity.

Methods: : Data collections have been done using databases: PubMed, Nature and Science Direct. To compare and summarize the different diagnostic methods of HDFN, books and articles that have been published by 2018 are studied.

Results: The methods used to diagnose HDFN are often invasive, non-specific, or can exacerbate the disease. Also, the treatments performed for the fetus are not completely effective or free of complications. Therefore, the use of NIPD test is important because the required sample is taken non-invasively from the mother in the first trimester of pregnancy and does not cause complications of other diagnostic methods. Also, the specificity and sensitivity of the procedure in the diagnosis of trisomy, preeclampsia and HDFN is close to 100%.

Conclusion: In forecasting HDFN using the NIPD test, a specific biomarker of cff DNA is investigated. Cff DNA is pieces of fetal DNA that are the result of cell denaturation and are passed through the placenta into the mother's bloodstream. This marker reaches its peak in 11 to 13 weeks of pregnancy and minimizes the time of disease prediction compared to other methods. Another benefit of this method is the reduction of errors in the prevention of mothers with Rh- because for all these people without an accurate diagnosis of fetal Rh, prophylaxis with RHIg is prescribed, which has its effects on the mother. In some cases, it leads to exacerbation of allergies or disease transmission. Some theories suggest that RHIg may lead to lysis of embryonic RBCs due to its ability to cross the placenta.

Keywords: HDFN, hemolytic disease diagnosis, cff DNA, NIPT

Non-pharmacological Interventions that Promote Sexual Function in Postmenopausal Women: A Scoping Review (Review)

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Introduction: Menopause is a physiological phenomenon that is associated with physical, psychological, and especially sexual complications. Sexual function is an essential part of women's lives, and changes in it, especially during menopause, can affect women's health. Various pharmacological and non-pharmacological interventions have been performed to improve the sexual function of postmenopausal women. Due to the different side effects of drug therapies such as hormones therapy and the conversion of postmenopausal women to non-drug therapies, the present study was conducted with the aim of reviewing non-pharmacological interventions affecting the sexual function of postmenopausal women

Methods: The present study is a scoping review. In this study, the researcher performed a comprehensive search of Google Scholar, SID (Scientific Information Database), PubMed, Scopus, Cochrane Library, Science Direct, MagIran, Web of Science, using the English keywords of Menopause, Postmenopause, Premenopause, Perimenopause, Climacteric, Non-pharmacologic Intervention, Psychological Intervention, Counseling, Education, Sexual Function, Sexual Health, and their Persian equivalents were searched. A total of 871 articles were collected from 2000 to 2020. Then, 482 articles due to duplication, 247 articles due to irrelevance, 79 articles in the abstract screening stage, and 43 articles in the full-text review stage were deleted. Finally, 20 articles were used for writing.

Results: Findings of the present study in the field of review of non-drug interventions that promote sexual function in postmenopausal women were divided into three general categories: The category of educational interventions includes (educational interventions based on sexual function promotion and sexual satisfaction), The category of psychological interventions includes (study of hypnosis-based relaxation, self-efficacy, group support, counseling based on emotion regulation, and counseling based on promoting sexual function in couples), The category of complementary medicine interventions includes (aromatherapy, dietary supplements, and pelvic floor muscle exercises).

Conclusion: Since menopause affects women's sexual function, and according to the findings of the present study on the effectiveness of educational, psychological, and complementary medicine interventions in improving postmenopausal women's

sexual function, use the non-pharmacological interventions mentioned by health care providers. It is recommended to strengthen and enhance the sexual function of postmenopausal women.

Keywords: sexual function, menopause, non-pharmacological interventions

Nutrition and renal health in preterm infant (Review)

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Introduction: Nutrition can affect the function of many organs, such as the kidneys. Premature birth occurs in almost10% Of all births, often associated with low birth weight (LBW). Low birth weight (LBW) is associated with a decrease in the number of nephrons at birth and kidney disease such as nephrocalcinosis (NC). We want to examine the relationship between nutrition and kidney health and how it affects the development of kidney disease.

Methods: We searched PubMed and Google Scholar databases for related articles. 102 articles have been reviewed, 10 of which are relevant.

Results: NC in premature infants is associated with impaired renal tube function and kidney length (KL).Crystallization is also common in all minors.In addition, intrauterine growth restriction and LBW are associated with a decrease in the number of nephrons.Nutrition in early life has a major impact on health. Excessive consumption of calcium and phosphorus, which is currently prescribed for premature infants in the first 4 weeks, poses a risk of developing NC.(6) Increasing the concentration of sodium in the blood and reducing the number of nephrons increases blood pressure.(4)Some studies have shown that the quality and quantity of postpartum nutrition, including calories, protein, and food content, may plan the number of nephrons and kidney function. In addition, mothers who give birth to premature babies are at high risk for long-term hypertension, kidney and cardiovascular disease, and subsequent complicated pregnancies.

Conclusion: The results suggest that the quantity and quality of postpartum nutrition affects renal function in premature infants.Therefore, prevention of preterm labor, improvement of girls' education and optimization of maternal weight and nutrition and various interventions including calcium and zinc supplements in the mother will be useful in reducing the risks.

Keywords: Nutrition, preterm infant, nephrocalcinosis, kidney

Nutritional disadvantages of diamino acids and correlated amino acids (Review)

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Introduction: : Processing of the protein-containing food industry by heating and increasing or decreasing the pH would change the taste as well as eliminate microorganisms. Eventually it will increase the digestibility and safety of food. But this process has some disadvantages and could lead to two very important chemical changes. One is the formation of cross-linked amino acids such as Lysinoalanine and the other is the conversion of free amino acids in the combination of proteins to diamino acids. Both of these unwanted chemical compounds have the potential to induce toxicity and decrease nutritional value of the processed food. They are classified as food chemical contaminants. The increase in the appearance of diamino acids and correlated amino acids in food depends on its processing conditions. Conditions such as pressure, ion strength, and catalysts such as heavy metals (copper and iron), pH, heat and processing time. Amino acids play a key role in increasing the nutritional value of foods and health, but diamino acids do not have the ability to be metabolized and consumed in the human body. Therefore, in foods that have high amounts of right-handed isomers (diamino acids), they may have high protein in chemical analysis, but this does not mean that their nutritional value is just as high. Bonded amino acids exist in both intramolecular and extramolecular correlations and are proteins that form covalent bonds between their own polypeptide chains or with other proteins. Apart from the negative effects, correlated proteins have useful applications in the food industry, such as changing physical properties such as viscosity to improve food quality and marketability. Food companies today are aware of the consequences of improper processing of protein-containing foods and are preventing the so-called drastic processing of food.

Methods: Using keywords: Dioamino acids, Paired amino acids, Food, etc. Browse the articles, journals, and books to gather information about nutritional disadvantages of diamino acids and correlated amino acids

Results: During the surveys; After feeding a group of rats with foods containing diamino acid, it was observed that rats that had high amounts of diamino acid in their diet; Growth rate was significantly reduced compared to rats on a normal diet. The main reason for the formation of correlated proteins in food is the sudden change in pH. Food processing though in cases such as cereals, with the loss of anti-nutritional substances such as tannins; Vitamins such as riboflavin and niacin are also helpful in detoxification, but research has been done by adding lysinolanin

to rat diets; The growth suppression effects of this correlated protein were demonstrated in mammals.

Conclusion: Diamino acids that are almost rare in raw foods; Food processing is formed by a sudden change in pH, heat and processing time. Diamino acids by reducing the digestibility of the food and also reducing the nutritional value of that food; The effects of non-standard food processing are well illustrated. They also prove their nutritional harm by inducing oxidative stress in cells and nephrotoxicity (toxicity to kidney nephrons). The amount of correlated amino acids is directly related to the intensity of food processing; It causes nephrocytomegaly in rodents (not yet proven in humans) and also, like diamino acids, reduces the nutritional value of food.

Keywords: Dioamino acids, paired amino acids, food.

Occult hepatitis B infection (OBI): a debate on HBV vaccination paradigm (Review)

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Introduction: Chronic HBV infection endangers the lives of 257 million carriers worldwide as it may lead to severe conditions such as liver cirrhosis or hepatocellular carcinoma. The current yeast-derived vaccines are the most effective strategy to prevent hepatitis B diseases. However, along with the growth of research around occult HBV infection (OBI) in immunized individuals and the residual risk of mother-to-child-transmission in 10-30% of infants born to HBsAg positive mothers, there is increasing concern that HBV vaccines cannot guarantee complete protection. The aim of this study is to provide better insight into the impacts of the general HBV vaccination program on OBI and to address the major drawbacks of current vaccines.

Methods: We searched PubMed, Scopus, and Web of Science databases to identify studies on OBI among vaccinated populations. A total of 73 eligible studies published between 2004 and 2018 were identified.

Results: We found several studies reporting the emergence of OBI in fully vaccinated individuals of both the general population and high-risk groups such as newborns of HBsAg positive mothers. Low-level anti-HBs and high maternal viral loads in MTCT cases as well as vaccine escape mutants and heterologous HBV genotypes are the factors contributing to vaccine failures.

Conclusion: Further research is required in order to clarify the precise impact of active immunization on the emergence of OBI in the vaccinated population. However, what is certain is that with the development of more potent HBV vaccines, the eradication of HBV would be more imaginable.

Keywords: General population; Mother-to-child-transmission; Hepatitis B vaccine; Chronic Hepatitis B

Oral Administration of Probiotic Enterococcus Durans Ameliorates Experimental Autoimmune Encephalomyelitis in Mice (Research Paper)

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Introduction: Multiple sclerosis (MS) is a myelin-degenerating autoimmune disease in the central nervous system (CNS). Experimental autoimmune encephalomyelitis (EAE), due to its clinical and pathologic features similar to multiple sclerosis, is widely used in many studies of this disease as an effective and similar model. Probiotics, including lactobacilli, are known to induce immunomodulatory activity with promising effects in inflammatory diseases. In this study, we tested the potential of Enterococcus durans and three various strains of lactobacilli (lacto-mix), Including L.rhamnosus, L.casei, and L.plantarum for prevention of EAE features.

Methods: C57BL/6 female mice were inoculated with (MOG35-55) / (CFA) to induce EAE. Different groups (five groups: n = 6 in each group) of animals received saline or probiotics by oral gavage with 200 µl of lactobacilli (1.5 *108 CFU/ml) for 2 week before the immunization and during the test for one month.

Results: Histopathological studies showed an increase in infiltration of inflammatory cells and destruction of the myelin membrane in the EAE group but a decrease in the probiotic-treated animals. Pro-inflammatory cytokines (IL-17 and IFN-γ) concentration in the supernatant of the brain and spinal cord tissues showed a significant increase in the EAE compared with the normal saline group ($p < 0.01$), while in the spinal cord tissue there was a decrease in IL-17 in those animals treated with the Lacto-mix and Edu + Lacto- mix ($p < 0.01$) and a significant decrease in IFN-γ in those animals that received Edu ($p < 0.05$). Western blot analysis of MMP-9 and MBP proteins showed a decrease and increase in treatment and EAE groups, compared to the normal control group respectively.

Conclusion: our data suggest that probiotic Enterococcus durans and lacto-mix had a preventive effect against EAE but further studies are needed to clarify the exact mechanisms and their application in preclinical and clinical trials.

Keywords: MS, EAE, Anti-inflammatory, Antioxidant, Probiotic, Enterococcus durans

Outcomes and Challenges associated with In vitro Fertilization in Women with Polycystic Ovary Syndrome: A review study (Review)

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Introduction: Polycystic ovary syndrome (PCOS)is the most common endocrine disorder in women of childbearing age. There are many challenges regarding the quality of oocytes in these individuals. Therefore, this review study aimed to investigate the consequences and challenges associated with in vitro fertilization in women with polycystic ovary syndrome.

Methods: For related studies, the Persian SID and Magiran databases and Pubmed, Scopus, Elsevier, Weily online library, Sciences Web of Science databases and Google Scholar search engine were used for the period 1990–2019. To obtain all articles in Persian and English ,the keywords of Polycystic ovarian syndrome, in vitro fertilization, Polycystic ovarian morphology ,IVF outcome, Oocyte donation, Oocyte competence ,Pregnancy, and their Persian equivalent are used separately or as possible combinations. From 450 articles, 17 were eligible and selected for this study.

Results: The results of various studies suggesting major challenges in this group of women including gonadotropins need and hormone-related changes, ovarian hyperstimulation syndrome (OHSS), clinical pregnancy rates, pregnancy outcomes and the risk of miscarriage, the quality of oocytes in women with polycystic ovary syndrome undergoing in vitro fertilization and the issue of egg donation in this group of women. However, fetal loss, clinical pregnancy and live birth rates are no different from other women.

Conclusion: Due to concerns about pregnancy in women with PCOS, closer monitoring of these pregnancies is important, it also appears that the presence of PCOS in donors does not affect the rate of pregnancy or implantation and the number of embryos transferred in ovarian donation programs. As a result, women with PCOS should not be excluded from egg donation programs.

Keywords: Polycystic ovary syndrome, in vitro fertilization, Pregnancy, Egg donation, in vitro fertilization

Overexpression of miR-146a and TNF-a increase the risk of breast cancer (Research Paper)

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Introduction: The NF-kappa B (NF-κB) signaling pathway can help to explain the link between inflammation and cancer. MiR-146a influences the function of NF-κB and contributes to different aspects of tumorigenesis. Tumor necrosis factor-alpha (TNF-α) has been shown to promote tumor initiation, promotion, as well as invasion and metastasis as necessary tissue architecture for tumor development through activation of NF-κB. In this case control study, we evaluated the TNF-α and miR-146a mRNA expression pattern in breast cancer (BC) to shed light on some aspects of breast cancer in the molecular level.

Methods: Fifty-two women diagnosed with BC (44 DCIS; 8 LCIS) and 52 healthy women as controls were enrolled in the present study. The expression of the TNF-α and miR-146a genes was determined by reverse transcription quantitative-polymerase chain reaction (qRT-PCR). All cases were examined for the receptor of estrogen and progesterone using Allred scoring and immunohistochemistry for TP53. Hematoxylin-eosin staining was used to differentiate different types of BC.

Results: Patient women presented with increased TNF-α and miR-146a expression compared to controls ($P < 0.0001$). The expression of TNF-α among women above 50 years was significantly higher compared to controls, while the expression of the mRNA expression of miR-146a in women below 50 years was significantly higher than controls.

Conclusion: The data obtained from the present study demonstrated that upregulation of TNF-α and miR-146a expression may involve in tumor initiation and promotion by facilitating malignant cell transformation of breast cells through NF-κB activity.

Keywords: Breast cancer, miR-146a, TNF-α, NF-κB signaling pathway, Gene expression

Overview in the use of nanosystem to Target Cancer Metastasis (Review)

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Introduction: The systemic spread of malignant cells from a primary site, a procedure denominate metastasis indicate a global challenge in cancer treatment and cause of cancer- relevanted fatality that accounting for 90% of cancer deaths. The precipitate development of cancer research has naked new mechanistic network and pathways that promote metastasis

Methods: As a result, a major number of antitumor factors have been expand for their antimetastatic efficacy. Notwithstanding their cytotoxic effects on tumor cells and antitumor activities in preclinical research in vivo, only a few have shown powerful antimetastatic activities in clinical trials. On the other hand rapid growth in nanotechnology toward the development of nanomedicine agents holds massive promise to improve therapeutic approaches against cancer

Results: They have been analyzed for different clinical applications, such as drug carriers, gene delivery to tumors, and contrast agents in imaging. A wide range of nanomaterials based on organic, inorganic, lipid, or glycan compounds, as well as on synthetic polymers has been utilized for the development and improvement of new cancer and antimetastatic therapeutics

Conclusion: This review highlights the research on the applications of nanoparticles in the treatment of metastatic cancer and antimetastatic strategies, particularly on the possible effect on cell stabilization, growth inhibition, conditional interaction with adhesion molecules to develop nanotechnology-based tools for treating metastatic.

Keywords: Nanoparticles, antimetastatic strategies, nanomedicine , malignant cells

PD and steam cells therapy (Review)

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Introduction: Parkinson's disease (PD) is a neurodegeneration disorder caused by the destruction of dopaminergic neurons in the midbrain, and the cause of this degradation is not yet known. But factors such as environmental pollution, age, toxins and genetic factors to be involved in this destruction. Cell- replacement therapies showe an attractive prospect for treating PD. With relatively localized neural degeneration, similar to spinal column injury, PD presents a better candidacy for cell therapy when compared to other diffuse degeneration found in Alzheimer's or Huntington's Disease.

Methods: Transplantation of midbrain dopaminergic neuron (DA) precursors from allogeneic fetal tissue was performed to the striata of individuals with PD. The first-in-human clinical studies provided proof of concept that tissue could be implanted into the brains of patients with no overt negative effects at the target site of transplantation, but variable clinical benefits were observed. Other sources of cells for transplantation have included autologous adrenal medullary tissue as a source of DA derived from neuroendocrine chromaffin cells, autologous carotid body tissue as a source of DAergic glomus cells and retinal pigmented epithelial cells as a source of levodopa. However, transplants of cells other than authentic fetal ventral mesencephalon (VM) DAergic neurons have failed to demonstrate key requisite properties. In particular, the rationale for transplanting adrenal medullary tissue, which is based on the fact that neuroendocrine chromaffin cells can produce DA, has been questioned. Importantly, the open-label studies demonstrated that fetal VM was the only cell source that conferred the potential for clinical improvement and, notably, for graft survival and function as demonstrated by clinical measures, neuroimaging and post- mortem histo logical analysis. However, the outcomes of fetal tissue-derived cell transplants in individuals with PD have been variable, in part owing to the limitations of fetal tissue as a cell source, relating to its availability and the lack of possibility for standardization and to variation in methods. Neurosurgical implantation of pluripotent cells poses the risk of an innate immune response and tumorigenesis. Precautions, therefore, must be taken to ensure cell line quality before transplantation. Advances in developmental and stem cell biology have allowed the development of cell-replacement therapies that comprise dopamine neurons derived from human pluripotent stem cells (hPSC), which have several advantages over fetal cell-derived therapies. Current techniques focus on induced pluripotent stem cells (iPSCs) because they can be matched with donors using human leukocyte antigens, thereby reducing the severity and risk of immune rejection. Sourcing cell therapy with iPSC lines provides ethical advantages because these stem cell lines do not require the sacrifice of human zygotes and genetically-specific drug trails can be tested in vitro without lasting damage to patients. Transplantation of hPSC- derived DAergic neuron precursors to the striatum is predicted to generate more robust and consistent outcomes than previously tested regenerative therapies using fetal VM tissue. In hopes of finally

slowing the progression of PD or re-establishing function, iPSC lines can ultimately be corrected with gene therapy and used as cell sources for neural transplantation for PD. The first human clinical trial using iPSC cell therapy transplantation for patients with moderate PD was performed in 2018. For cell therapy to be optimized, effective and clinically relevant for a wider range of symptoms, key limitations must be addressed in the future using emerging technologies and new disease insights: as trials progress, optimal and probably individualized dosing and spatial delivery schemes, possibly based on PET biomarkers that quantify and map out existing DA inputs, will improve. In addition, adjunct interventions to increase cell survival, enhance physiological synaptogenesis and promote development of 'normal' neuronal controls on the engrafted cells are likely to be put in place. This could be attempted, for example, using gene modification to express neurotrophic or other factors, or by simultaneous delivery of adjunctive therapeutics

Results: Over the past few decades, rapid advances in stem cell technology, including development of robust differentiation protocols and manufacturing processes, have facilitated the development of a first generation of hPSC-derived DA neuron technologies that are now in the pipeline for first- in-human clinical trials. Although there is not yet a valid evidence at a disease-modifying treatment, stem cell technologies have the potential to be at the forefront of such PD treatments in the future.

Conclusion: Over the past few decades, rapid advances in stem cell technology, including development of robust differentiation protocols and manufacturing processes, have facilitated the development of a first generation of hPSC-derived DA neuron technologies that are now in the pipeline for first- in-human clinical trials. Although there is not yet a valid evidence at a disease-modifying treatment, stem cell technologies have the potential to be at the forefront of such PD treatments in the future.

Keywords: Parkinson's disease cell- replacement steam cells

Personalized medicine improves the patients' treatment, Look at ADHD (Review)

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Introduction: Methylphenidate (MPH) reduces hyperactive-impulsive symptoms common in children with attention-deficit/hyperactivity disorder. however, response and tolerability varies widely. We hypothesized gene variants may moderate MPH effects in children ADHD.

Methods: The onset of personalized medicine goes back to Avicenna when he points out that the diseases caused by the imbalance of the main body fluids. Now, personalized medicine actually means "right treatment for right person at right dose and right time". Today, due to different responses of patients to drugs, studies in personalized medicine has been developed and are in progress. The most important factors responsible for different responses to treatment are genetic variations. Pharmacogenomics deals with the influence of acquired or inherited genetic variations on pharmacokinetics and pharmacodynamics of drugs. Neuroleptics and psychotropic need to be personalized because of their side effects. Pharmacogenetic tests has the potential to improve clinical outcomes through increased efficacy and reduced toxicity and side effects. ADHD is the most commonly detected mental disorder of children. Children with ADHD may be hyperactive and unable control their instincts. Or they may have trouble paying attention. the underlying pathomechanism of ADHD are not fully understood. The first line treatment of hyperactivity symptom is methylphenidate but the response of the patients is widely variable. MPH works by preventing the reuptake of dopamine (DA) and norepinephrine (NE) through inhibition of the DA (SLC6A3) and NE transporters (SLC6A2), resulting in an increase in extracellular DA and NE. ¬the studies showed that genetic variants that is related to Neurotransmitter synthesis and degradation ‹Neurotransmitter reuptake ‹Neurotransmitter receptor binding ‹ Neurotransmitter release ‹Neuronal/synaptic plasticity and synaptic effectors and Downstream neurotransmitter effects affect on the response to the methylphenidate. So far, numerous attainments have been done in this field, but there are contradictory results on the impact or ineffectiveness of such variations in responses to the treatment. Despite many efforts on finding effective factors related to methylphenidate treatment, patients still suffering from drug side effects. Therefore, further studies in this field needed to determine effective biomarkers to improve ADHD patients' treatment.

Results: Some gene variants demonstrate different response to the MPH.

Conclusion: Our knowledge about the gene variants that affect on methylphenidate response help us to manage the symptom of ADHD better as compared to before.

Keywords: ADHD-Methylphenidate-genetic variants

Phenotypic and Genotypic Detection of AmpC Enzymes(MOX and CIT) in Clinical Isolates of Escherichia coli (Research Paper)

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1.
2.

Introduction: AmpC β-lactamase enzymes cause multi-drug resistance. The diagnosis of these enzymes in clinical isolates of bacteria is important in epidemiological, research Studies and hospital infections control because plasmid genes can be transmitted to other organisms in the hospitals The purpose of this study is detection of AmpC enzymes (MOX and CIT) in the isolated strains of E. coli in three educational hospitals in Hamadan (Iran).

Methods: 102 strains of E. coli and were isolated from the three hospitals in Hamadan from March to September 2017. The isolated gram negative bacteria identified by using common biochemical tests. Antibiotic sensitivity of isolated strains was studied by standard disk diffusion method and based on CLSI protocol .To detection of phenotypic AmpC activity, the AmpC detection disks were used. The clinical isolates with MIC ³ 8 µg/ml for cefoxitin were included for evaluation by AmpC diagnosis disks. To detect genes encoding for AmpC PCR method was used.

Results: : Sixty eight isolates (66.6%) were resistant to third generation cephalosporin and of these 61 (59.8%) isolates had MIC ³ 8 µg/mL to cefoxitin. All 68 isolates were analyzed by AmpC detection disks, of which 10(14.7%) isolates were AmpC- β-lactamase producers. By PCR method, 24 (35.2%) isolates had cit, 46(67.6%) for mox genes.

Conclusion: High resistance to cephalosporins has been observed among the clinical isolates. Due to the possibility of plasmid transferring of ampC genes between bacterial, changing consumption patterns of antibiotics and the treatment protocol is necessary. The results of this study suggested that physicians should pay attention while prescribing antibiotic and send the sample to laboratory for the antibiogram tests so that the best medical choice is given to the patients. The emergence of plasmid-mediated AmpC and ESBL β-lactamase producing E. coli and attitude possible risk to the spread of antibiotic resistance in the clinical situations.

Keywords: Escherichia coli, AmpC, Multi-Drug Resistance, β- Lactamase

Possible Therapeutic Methods of Infection by COVID–19 (Review)

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Introduction: The COVID-19 epidemic disease caused by acute respiratory syndrome coronavirus 2 (SARS–CoV-2) is a big challenge to find effective medicines in prevention and treatment. According to the rapid pace of the spread of this disease, changing the pathogenesis of the virus, and the new information that is declared daily about the infection of the virus, physicians need correct evidence to produce appropriate drugs and vaccines for this disease.

Methods: In this review study, four databases include Google scholar, pub med, Scopus, and Science direct; and keywords like COVID-19, SARS-COV-2, treatment, and drug used for collecting the information. Articles that did not have our purpose omitted from the study process.

Results: There are no effective therapeutic methods for treating COVID-19 infection at present time. The rapidly developing science about SARS-CoV-2 virology has prepared a significant number of potential medicinal targets. Now, more than 150 different drugs are being scrutinized. The promising remedy is Remdesivir which has strong performance against SARS-CoV-2, but has not been confirmed by the United States Food and Drug Administration and is being continuously tested in randomized experiments right now. The other drug is Oseltamivir its effectiveness is doubtful. Two other drugs consist of Lopinavir and Ritonariv which used to treat HIV and AIDS, but there is not much evidence to appoint their effect on COVID-19 infection treatment. Hydroxychloroquine has previously been widely used to treat COVID-19; however, because the accumulation of these drugs in the lungs is not sufficient to fight the coronavirus, the use of this drug was also limited. Corticosteroids are not recommended either. The present clinical evidence does not support the cessation of the angiotensin - converting enzyme nor angiotensin receptor blockers in patients afflicted with COVID-19. On vaccine, extensive researches have begun since the outbreak of the disease, and conclusive stages have to be traversed to ensure its effectiveness and safety.

Conclusion: The COVID-19 epidemic disease is the biggest global public health crisis in this generation and potentially ever since the outbreak of the flu epidemic in 1918. The rate and volume of clinical experiments, which have begun to examine potential therapeutic methods for COVID-19, indicates the need and ability of researchers trying to find suitable medicine or vaccine with high quality for this disease. Anyway, there are no complete therapeutic methods for this disease.

Keywords: COVID-19, SARS-COV-2, epidemic, treatment, and drug

Postoperative Cognitive Dysfunction (POCD) after Oncological Oral and Maxillofacial Surgery (Review)

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Introduction: Introduction: POCD is known as a decrease in cognitive function based on preoperative to postoperative, neurological and psychological tests, which in some patients It will last more than 30 days and, in some patients, more than 6 years. Gender, age, duration of anesthesia, trauma, surgery, and hemodynamic changes that lead to ischemia are considered as risk factors of POCD. Cardiac surgery and some orthopedic procedures can cause POCD in patients. Oral surgeries have shown an increase in serum NSE and S100B levels after surgery; there is also a link between their increase and the incidence of POCD, so it can be said that POCD occurs after oral surgery. POCD can have influence on person's concentration, memory, learning ability, emotions, movements as well as the quality of recovery after anesthesia, quality of life and Duration of hospitalization. It can even affect the mortality of patients after surgery. aim: The aim of this study was to evaluate the effect of POCD after oral and maxillofacial surgeries in patients with oral cancer, on the patient's recovery.

Methods: Method: To this narrative review we limited our search to 2015-2020 and considered the studies that met our exclusion criteria. Then we assessed the three studies known to be relevant to our topic from six English articles by searching four databases such as: PubMed Central, Science Direct, Cochrane and Google Scholar by medical subheadings (MeSH) of oral cancer, maxillofacial cancer surgery, POCD, incidence, epidemiology, risk factors. The exclusion criteria are relating title and abstract and content of article to POCD after oral and maxillofacial surgery. The measure of this study was that we wide examined the factors contributed to the occurrences of POCD in patients after Oral and maxillofacial surgery.

Results: POCD can have different causes. Factors like gender, age, trauma, duration of the surgery and even the patient's level of education might affect the occurrence of POCD. In this study the results of three articles were considered. Two of them directly studies patients with a total group of 935 participants. Out of 935 who were studied, only 222 patients could successfully finish the test. 46 of these were in the study group, and 176 others were in the control group.

Participants' average age was 52.67, including 106 females (47.74%) and 116 males (52.25%). 49 participants (22.07%) were frequent smokers and 82 of them (36.93%) were nonsmokers. 34 participants (15.31%) were alcoholic and 93 (41.89%) occasionally consumed alcohol. 21 participants (9.45%) were diabetic. We understood that factors like diabetes, smoking, alcohol may not be very effective in the occurrence of POCD. Although some articles claimed that Dementia is the most significant factor associated with POCD, the etiology of it is still unclear.

Conclusion: Conclusion: POCD can highly occur after surgery (especially orthopedic and cardiac surgery). It can have great influence on patient's concentration, memory, learning ability, emotional state, movements as well as the quality of recovery after anesthesia, quality of life and duration of hospitalization. It can even increase the mortality of patients after surgery. According to the results of the study, we found that dementia is the most significant factor associated with the occurrence POCD but we are not certain whether diabetes, smoking and consuming alcohol can significantly change the occurrence of POCD. It is suggested that optimized anesthesia guided by processed EEG indicates in patients with dementia could reduce the risk of POCD. Further studies with more participants are required to elucidate the right strategies for reducing the incidence of POCD after oral surgeries.

Keywords: POCD, postoperative cognitive dysfunction, surgery, oral cancer, maxillofacial cancer

postpartum depression and ways to prevent it. (Review)

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Introduction: Postpartum depression is one of the most common postpartum mental disorders that a mother experiences in a few weeks, months, or even a year after the birth of her baby. This depression can also affect mothers who have given birth before or mothers who have adopted children. With symptoms such as crying for no reason, feeling sad and lethargic and helpless most days, feeling guilty, feeling worthless and hopeless, thinking about suicide and scary thoughts. And cause serious problems for the mother of the child and the family, so this article will discuss solutions to reduce and Prevent this mental disorder.

Methods: According to the findings, problems such as family history of depression and mental illness, stressful events in the last year, social inequalities such as inadequate housing or insufficient income to support the child, experience of violence and abuse, etc., are the causes of postpartum depression. Therefore, by taking the mother's history and family history before childbirth and providing services appropriate to her social and psychological condition, such as reducing labor costs, prescribing low-dose antidepressants to increase serotonin, and explaining systematic programs. The basics of "postpartum diarrhea".

Results: 10 to 16% of women with postpartum depression begin to experience this condition during pregnancy. The prevalence of postpartum depression in different societies varies from 5% in Denmark to 36% in Chile. In internal studies, up to 2.22% in Abadan and 5.30% in Tabriz has been reported. The pattern of postpartum depression in Iran is 3 times more than developed countries.

Conclusion: Considering the apparent prevalence of postpartum depression and its serious risks on the health of mother, child and family, and by examining the patterns of internal and external prevalence, we understand the impact of social factors. Especially in high-risk groups, as well as the supportive roles of family and friends on mental health.

Keywords: Postpartum depression , Social factors

Pre-incubation with Kisspeptin improves the adverse effects of the freeze-thawed Human Ejaculated sperms (Research Paper)

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Introduction: Spermatozoa cryopreservation results in reduction of sperm quality. Kisspeptin (KP), as an antioxidant, has beneficial effects on the sperm functions. The objectives of this study were to determine the mitigating impact of KP on detrimental effects of the sperm freeze-thawing process and compare it with glutathione (GSH), as the positive control.

Methods: Thirty normal semen samples, prepared by swim-up procedure, were divided into three aliquots: negative control, without any treatment; positive control receiving GSH; and experimental aliquot treated with KP for 30 min. All aliquots were cryopreserved, and then thawed after 48hr. Sperm motility was assessed according to WHO guidelines. Acrosomal reaction and capacitation were evaluated by FITC-conjugated Peanut agglutinin (PNA), Wheat germ agglutinin (WGA), and Concanavalin A (ConA); the percentage of the positive cells was evaluated by flowcytometry. Sperm DNA quality was evaluated by Acridine Orange, Aniline Blue, Chromomycin A3, and TUNEL staining methods. Statistical analyses were performed using ANOVA and LSD.

Results: KP supplementation improved the motility and led to an increase in the percentage of capacitated and acrosome-intact sperms compared with both controls. Freeze-thaw procedure damaged DNA integrity severely, and KP pre-treatment significantly reduced the frequency of apoptotic sperms along with those with histone – protamine substitution impairment.

Conclusion: Pre-exposure of the sperms to KP can protect the sperm quality including motility and DNA integrity against the detrimental influence of freezing and thawing. Therefore, it can be considered as a good pre-additive substance to control the sperm quality during freezing and thawing procedure.

Keywords: Kisspeptin, motility, DNA integrity, Cryopreservation, Lectin histochemistry

Precision Medicine for Rare Diseases: Classifying Patients with Limb-Girdle Muscular Dystrophy Aimed in Proposing Applicable Therapeutic Strategies for Each Subtype (Research Paper)

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Introduction: Since therapeutic approaches are rarely developed for single individuals, it is necessary to assign each drug or therapeutic strategy to a subgroup of patients. Precision medicine (PM), also known as personalized medicine, refers to the understanding diseases at a deeper level in order to develop more targeted therapies. Herein, we demonstrated how PM can be beneficial for patients with “Limb-Girdle Muscular Dystrophy” (LGMD). LGMD belongs to a heterogeneous group of diseases called Muscular dystrophies which are characterized by progressive muscle wasting. There are 9 major types of muscular dystrophy, all of which cause muscle weakness, but the areas affected and the severity of the symptoms are different. Among these various types, Duchenne is the most common, and limb-girdle is the most heterogeneous disease with more than 30 subtypes depending on the different genes involved. LGMD is caused by mutations leading to the abnormal protein synthesis in the various parts of the muscle fiber including the nucleus, sarcoplasm, sarcomere, sarcolemma, and extracellular matrix. In this project we aimed to classify patients with each subtype of limb-girdle, based on more detailed aspects such as mutation types, in order to propose applicable therapeutic approaches.

Methods: At first, we searched literature using the “Limb-Girdle Muscular Dystrophy” or “LGMD” keywords in Pubmed database. Totally, 1725 article were identified. Then we extracted potential therapeutic approaches from these articles. These data were subsequently categorized into 3 main therapeutic strategies: 1- Pharmacological approach 2- Antisense Therapy 3- Genome-Based Therapy Then we designed an algorithm based on different rules from each categories as an eligibility criteria to check whether an individual with a specific mutation in a specific gene, is a potential candidate for receiving any of these three therapeutic strategies. Additionally, we employed machine learning models based on the variants have been annotated in ClinVar database to predict the pathogenicity outcome of all variants cataloged in dbSNP. The algorithm for predicting proper therapeutic strategy was applied on all those variants predicted to be pathogenic.

Results: By applying our machine learning algorithm on all the variants reported in dbSNP for all the genes known so far for LGMD, we could determine potential pathogenic variants. Using our algorithm to predict proper therapeutic approaches we could propose appropriate strategies such as using glucocorticoids, anti-myostatin drugs, ASOs to target mRNA aimed in exon/multi-exon skipping and viral

vectors for precise gene-delivery for these variants. Some of the variants had more than one predicted approaches.

Conclusion: Due to high attrition rates, substantial costs and slow pace of new drug discovery or therapeutic strategy development, repurposing of old drugs and available therapeutic strategies is essential to treat diseases. On the other hand, despite necessity for investment in the development of treatments for people with rare disorders, the rarity of diseases makes them less attractive for pharmaceuticals. About a heterogeneous condition like limb-girdle muscular dystrophy it is even more difficult to find a cure for patients. Although not many studies have been performed on each subtype of LGMD, but various drugs and strategies have been proposed for this disease. We have classified LGMD patients to different subgroups that have differential features and treatment implications based on their mutation types in order to propose applicable therapeutic strategies for each subtype. This brings us closer to the treating and managing more LGMD patients.

Keywords: Precision medicine, LGMD, muscular dystrophy, classification, variant

Preparation and application of PVA/Gelatin/laminin Scaffold in Neural Tissue Engineering (Research Paper)

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Introduction: An example of a complex phenomenon in biology is the regeneration of nerves. If any impairment occurs in the nervous system, the recovery process will be difficult. Plus, malfunctions may occur in other parts of the body due to the fact that mature neurons cannot perform cell division. In this study, a novel neural tissue scaffold is introduced based on PVA/Gelatin/laminin to provide an alternative solution for this problem. In this method, we cross linked the PVA/Gelatin scaffolds physically using the freezethaw technique and performed a follow-up coagulation bath treatment. The gelatin/PVA solution was freeze/thawed and pre-frozen at different temperatures (i.e. -4, -80, and -196°C). Then, the scaffold was constructed using the freeze-drying method. Afterward, samples were covered with laminin protein. Next, to evaluate the effects of various parameters in the gradient temperature on the scaffold's morphology, Scanning Electron Microscope (SEM) was employed. To perform in vitro evaluation, the P19 mouse cells were differentiated into nerve cells on scaffolds. Finally, an immunofluorescence test was administered. As confirmed by the experimental results, this model can be applied as a suitable platform for neural tissue engineering.

Methods: 2.1. Materials For our study, gelatin was provided from Merck (Darmstadt, Germany), while MTT (3-[4.5-dimethylthiazol-2-yi]-2.5-diphenyltetrazolium bromide) and PVA (with molecular weight between 85000–124000 and alcoholysis~99%) were obtained from Sigma-Aldrich. Cell lines L-929 (mouse fibroblast cells) and P19 (mouse embryo carcinoma) were obtained the National Institute of Genetic engineering and Biotechnology, Tehran-Iran. Alpha minimum essential medium, Trypsin-EDTA, and the Fetal Bovine Serum (FBS) were obtained from Gibco BRL laboratories, Germany. 2.2. The Porous Gelatin/PVA Scaffold Preparation Process To prepare the necessary Porous gelatin/PVA scaffold, we employed aqueous solutions with 10% PVA (by weight) and various gelatin amounts, (i.e., 3%, 5%, and 7%, by weight). The (10%w/v) PVA solution was produced at 90°C. Next, the produced PVA solution was combined with gelatin with a ratio of 1:10 V/V. Once the mixture was homogeneous at T=60 °C, the mixture was cross-linked physically in three freeze-thaw cycles, including freezing for 24h at -4°C, thawing for another 24h at 21°C (room temperature). After that, the freeze-thaw cycle is repeated (due to the significance of PVA and gelatin-bonding hydrogen in creating 3D structures during the nucleation and growth) so that the gelatin porous hydrogels are prepared. Finally, lyophilization was carried out on the frozen samples for 24 hours. During the freezing process, when the chain of the polymer was frozen at -4, -80, and -196°C, nucleation was taken place inside the polymer solution, as shown in Fig 1.[12, 13] . Fig. 1. The process for the

Preparation of porous gelatin/PVA scaffold 2.3. Covering the scaffolds with laminin After the surface of the scaffolds is activated with plasma, to enhance the biocompatibility of the specimens with the cell, their surface is coated with laminin L2020. To this end, the samples were placed in a laminin solution with a concentration of 100 µg/ml for 4 h at 4 °C, immediately after activation with plasma. Once the surface of the scaffolds was bound with the laminin, they are washed several times using a PBS solution. Then, the samples were stored in the refrigerator for cellular culturing. 2.5. Analysis and Characterization 2.5.1. Scanning Electron Microscopy (SEM) The scanning electron microscope employed for capturing the images in this study was an AIS-2100, by Seron Technology, Korea. Plus, examinations were performed at room temperature. Sputter coating with gold was performed on samples before capturing the images to create conductive surfaces. For this aim, before performing the measurement, the samples were coated for 10 minutes with Au. Moreover, horizontal and/or vertical cross-sections were prepared via cutting the N2(l) to facilitate observation of the inner structures of the scaffolds from different directions. Furthermore, before performing SEM observation at 15 kV, the samples were freeze-dried and coated with Au. 2.5.2. Measurement Method for the Cavities' Average Diameter An electron microscope was employed to perform the measurement for the average diameter of the cavities in the scaffold's structure. To this aim, 30 cavities were randomly selected from the images obtained from each sample, and their diameters were determined using image-j software, while their average diameters were determined accordingly. Moreover, porosity was found fully bound that facilitated food transfer. 2.5.3. Swelling To determine the ratio of adsorption for the Phosphate Buffered Saline (PBS) caused by the scaffolds produced, the samples dried in freeze-dryer were initially weighed. Next, the weighted samples were placed for 24 h on a shaker in PBS with pH = 7.4 at room temperature, while the PBS solution was refreshed multiple times. Using a paper filter, the water on the surface of the samples was removed. Then, the samples with solution were weighed, while the sample's absorbance ratio was derived according to the following equation: WPBS= (w2-w1)/w1*100 W1= The weight for the dry samples W2= The weight for the samples following immersion in PBS solution WPBS= PBS absorption percentage 2.5.4. Cellular attachment The reaction occurred between the scaffold and the cell culture was investigated during a number of in vitro cell culture trials. In these experiments, L929 mouse fibroblasts cells were cultured in culture medium (RPMI-1640) containing penicillin (100 µg /mL), streptomycin (100 µg/mL), and supplemented with fetal calf serum (10%). Prior to seeding, a cell suspension of 4×104 cells/mL was prepared. Samples were sterilized with 70% ethanol, followed by washing in the culture media. The samples were placed in a 6 well plate and cell suspension (5 mL) were added to each well keeping one well as control, plate was maintained in a CO2-controlled incubator for 48 hours at 37°C. When the incubation period was over, all samples were washed with phosphate-buffered saline solution. The cells were fixed using glutaraldehyde 2.5%. Finally, the cells were dehydrated by ascending grade of ethanol at 60, 70, 80 and 95%. 2.5.5. MTT Assay For the cytotoxicity test of the MTT, we used the L929 mouse fibroblast cells. First, a general examination was performed on the cells to ensure their proper condition. This task was carried out via observing the cellular proliferation, the morphologic structure of the flask containing the cell, and culture medium. Samples were sterilized with 70% ethanol and cell concentration was adjusted to 4×104 cell/ml.

Scaffolds were placed in a 24 well plate with control well without sample and to each well added 1 ml of cell suspension. After incubating at 37 °C in a 5% CO2 and 95% humidity incubator for 48 hours, 100 µL of MTT solution (0.5 mg/ml) was added to each well and incubated at 37 °C for 4 h. Following the removal of culture medium, acidified isopropanol was added in order to dissolve the formazan crystals. The optical density of formazan was measured spectrophotometrically at 570 nm using an ELISA plate reader. This absorbance value is proportional to the number of viable cells. Each of the samples and control was plated in triplicate MTT assays 24 hours. 2.5.6. Co-Culturing and Differentiation of Cells P19 mouse embryonic carcinoma cells were used in this study with the aim of confirming the scaffold's suitability for the task of neural cell growth. Following the acquisition of the cells, they were maintained and cultured based on the procedure described in Robertson.[16] The P19 cells were obtained in a frozen package. Therefore, their package was melted rapidly at 37°C. Then, the maintenance of the cells was carried out in a standard environment containing α-MEM (GIBCO, Germany) and 10% FBS. Plus, the cells were supplemented by 100µl/ml Streptomycin and 100 IU/ml Penicillin and were incubated at 37°C with 5% CO2. While the cells were in the incubation, the culture medium was changed in an interval of 48 hours until the cell number of 5×104 cell/ml was reached. Then, we transferred the cells to 100 mm bacteriological containers. The cultural medium utilized in this stage included α MEM (GIBCO), 0.3 µM retinoic acid (Sigma), and 10% FBS in 100mm bacteriological Petri dish. Cell culturing continued for four days and the medium was changed regularly every 48 hours. Several cell aggregates formed during the culturing period. Aggregations formed in the cell were mechanically separated and were transferred into specific cell cultures that contained scaffolds in an acidic and non-retinoic environment. This process continued for fourteen days. The cell's differentiation and growth during this period were observed using an optical microscope, while the negative control was considered the cultivation dishes in order to demonstrate the cell's growth. The culturing medium was discharged slowly after the 14th day in order to stabilize the cells grown on the scaffold. Then, to remove the dead cells, the scaffolds were washed for 5 minutes using PBS and dehydrated via immersing for 5 min in a range of ethanol-water solutions with 90, 80, 70, 60, 50, and 100% v/s. Then, we washed the samples for another 5 minutes. For the final drying, we maintained the scaffolds for 24 h in the ambient temperature. Finally, after the culturing and once the P19 cells were differentiated into scaffolds, we investigated the samples under SEM and using optical light microscopy techniques.[17] 2.5.7. Immunofluorescence Staining The aim of performing immunohistochemistry was to demonstrate a distinction between nerve cells and P19 cells on scaffolds using monoclonal antibodies. Washing the samples was carried out using PBS in a four-step process with intervals of 5 minutes. For duration of 30 minutes, 2% normal chloride acid was added to the samples in order to recover the antigen. Moreover, a borate buffer was added to the samples to neutralize the acid for a duration of 5 minutes. Then, the cells were washed via PBS. Furthermore, 0.3% triton was utilized for a duration of 30 minutes to make the cell membranes penetrable. 10% goat serum was added to the sample to act as an extra background color in order to block the secondary antibody response for 30 minutes. To this aim, using PBS, the diluted antibodies (1 to 100) were first added to the sample. Then, after the wetting medium was prepared, the sample was maintained in a refrigerator overnight at a temperature between 2°C and 8°C to

maintain the sample's wetness. The sample was removed the next day and was washed using PBS 4 times for 5 minutes. The secondary antibody, with a dilution range between 1 and 150, was added to the sample afterward. The obtained sample was then maintained for one and a half hours in an incubator in a dark place at 37ºC and was transferred to a dark room afterward. Next, the sample was washed four times and DAPI was added to it. This DAPI was removed immediately and was replaced with PBS. Finally, in order to confirm the markers, the obtained samples were observed under a 400mm lens using an Olympus Fluorescent Microscope.

Results: 3. Results and Discussion 3.1. Scanning Electron Microscopy (SEM) The freeze-drying method was utilized in this study to produce the PVA/gelatin scaffolds. As illustrated in Figure 2, the electron microscope utilized captured two types of vertical and horizontal images from the scaffold's cross-sections. As can be seen, a wide range of porosity in the structure exists in the images. The existences of an expanded porosity spectrum on the scaffold is indicative of initial temperature conditions, while the porosity distribution and the pore size is determined using the heat transfer. The effect of the temperature of the polymer on the scaffold's morphology is shown in Figure 2, where freezing at a constant concentration occurred in all samples. Moreover, since the polymeric chain density is in an inverse correlation with the temperature, it can be seen that increasing the wall's thickness was contributed to the temperature decrease in the solution, along with a decrease in the cavities' diameter. Hence, the parts in which the solvent maintained its cavity form remained smaller. Alternatively, as can be seen in Fig. 2a, the scaffolds that were produced using the freeze-drying method demonstrated large pores following freezing at -4°C. These pores were visibly noticeable in the cross-section between the cylindrical structures of a number of samples and the orientation of the scaffolds in a direction where the temperature gradient is applied. SEM observations illustrated in Fig. 2a and b revealed heterogeneous pores in a network structure with average inner-diameters of 250 μm. On the other hand, the pores in the scaffold that was prepared via freezing at the temperature of -80C had inner diameters of 85 μm, as can be seen in Fig. 2c, d. However, following freezing in N2(1), highly elastic scaffolds were prepared in the dried state by freeze-drying. Moreover, as can be seen in Fig. 2 e, f, homogeneous polygonal pores were observed. . Fig. 2. (a) SEM image from the 5% gelatin/10% PVA vertical cross-section in -4°C, (b) SEM image from the 5% gelatin/10% PVA horizontal cross-section in -4°C, (c) SEM image from the 5% gelatin/10% PVA vertical cross-section in -80°C, (d) SEM image from the 5% gelatin/10% PVA horizontal cross-section in -80°C, (e) SEM images from the 5% gelatin/10% PVA vertical cross-section in -196°C, (f) SEM images from the 5% gelatin/10% PVA vertical cross-section in -196°C. As can be seen in Fig. 2, the freeze-dried scaffolds' inner structure is affected by the freezing temperature via creating channels. The channel's direction is most likely identical to the direction in which the crystals of ice were formed. If the ice were formed without applying external forces, crystals of ice will form with a random form and with no dominant direction. However, if an external stress is applied to the crystals, (e.g. rapid cooling) the resulting ice will be oriented according to the temperature gradient that is induced within the gelatin/PVA scaffold. Therefore, the size of the pore may be reduced only alongside the scaffold's horizontal cross-section (i.e. in perpendicular to the gradient), while it will

be enlarged towards the scaffold vertical cross-section (i.e. along its axis). The most internal structure in the scaffold freezes at -196°C. In this layer, very thin connections exist between the walls, which are mostly due to the fact that at -196°C, the environment provides crystal orientation. Moreover, in this temperature, ice crystallization occurs randomly. A hypothesis regarding the structure of the inner porous modified via variation in the freezing temperature is illustrated in Fig. 2e and f. The varying thickness between walls and interconnections in the scaffold that was produced at -196°C is the cause for the difference in orientations and times. The polygonal shapes are particular shapes of ice. In specific, marks of freezing at low temperatures are similar to the freezing of liquid nitrogen. However, it is unclear whether the individual crystals were shaped into a new alignment from their initial spherulitic association and thus, experienced a reduction in size, or they melted when the liquid nitrogen penetrated and therefore, were formed with new orientations.[12] 3.2. Swelling An important factor in the design of the scaffolds is swelling since nutrients should penetrate the scaffolds, while the produced wastes generated by the cellular metabolism should exit. Therefore, in designing the scaffolds, the utilization of hydrophilic scaffolds is more desirable. As can be seen in Table 1, the high amount of inflation in these scaffolds is in relation to their highly porous structure. The level of water absorption in a scaffold for tissue engineering not only is effective in its structure and morphology, but it is also effective in the growth of the cells. If the absorption of the water was occurred generally within the gelatin hydrogel walls, then it is expected that the gelatin scaffolds that are prepared using high concentrations of gelatin would be capable of demonstrating higher levels of water absorption, but the experimental result obtained showed a contrary outcome. Therefore, we believe that the storage of the water occurred mainly in the porous space in the gelatin scaffolds. On the other hand, gelatin scaffolds that were prepared using low concentrations of gelatin possessed high porosity and large pore size and thus, offered more water storage capacity and yielded higher absorption. As confirmed by the experimental results obtained, absorption of water in the scaffolds is in relation to the scaffold's porosity that is adjusted via modifying the concentration of gelatin during the freezing process. -196 c -80 c -4 c Sample 3 Sample2 Sample1 PVA/gel 3% 848 727 414 1h 881 805 545 3h 968 914 748 6h 1547 1231 1120 24h Sample6 Sample5 Sample4 PVA/gel 5% 568 547 492 1h 807 684 589 3h 904 821 698 6h 1606 1556 1380 24h Sample9 Sample8 Sample7 PVA/gel 7% 371 344 302 1h 608 530 468 3h 855 789 741 6h 1363 1326 1331 24h 3.3. MTT Assay The results from the MTT test on scaffolds following 48 hours of culturing of the cells are demonstrated in Fig. 3. In specific, the cell's survival ratio on the scaffolds was measured using the formazan absorption rate. The cell's growth ratio can be seen at 570nm wavelength in the diagrams illustrated. Cell viability of 73% is a standard value for the nontoxicity of the biomaterial samples. All the samples produced in this study were biocompatible after 48 hours. This biocompatibility implies a lack of toxicity in L-929. The scaffold's cell viability and the L-929 cell contact were 85%. Fig. 3. MTT assay for a scaffold 3.4. Cell Culture The images obtained using the SEM can display the cell's overall interaction, structure, and adhesion to the samples. In the images obtained from the scaffold, the cell's interconnection is illustrated clearly. However, due to the porous structure of the scaffolds and their respective cell penetration, obtaining appropriate images is difficult. The penetration of cells to the porous structure is demonstrated in Fig. 4. However, it is worth mentioning that due to the non-uniform

surface of the structure, distinguishing the cells from the roughness over the surface is difficult. In any case, images with high quality were utilized in this article. Fig. 4. (a) The images captured using the optical microscope from the interaction between negative control and the fibroblast cells after 48 hours culture, (b) The sample from the scaffold after 48 hours culture. 3.5. P19 Cells Culturing and Differentiation The images captured using an optical microscope for the control samples (i.e. the samples that did not have scaffold) and the scaffolds after 8 and 14 days of culturing are demonstrated in Fig. 5. In this figure, cell aggregation is seen around the scaffolds. Moreover, it can be seen in the images for the 14th day that cellular connections were generally disconnected from the cells and made a connection to other cells. According to the images, over a course of 14 days, there was a complete change in the P19 cells and there was the emergence of the appendixes in the form of axons and neuronal dendrites. In addition, there were differences in terms of cellular expansion, growth, and cellular network expansion between the samples with scaffolds and the control. It can be concluded that no detrimental effects were seen from the presence of the scaffold on the activity of P19 cells of the mice. Finally, as confirmed from the results of the study, scaffolds are a biocompatible option for P19 cells. Fig. 5. (a) Interaction between P19 mouse cells and positive control captured by the optical microscope following 8-day culture, (b) scaffold sample following 8-day culture, (c) positive control following 14-day culture, (d) scaffold sample following 14-day culture. 3.6. Staining of Immunofluorescence and DAPI To this aim, the primary antibody was applied to the microtubule-associated Protein-2 (MAP2). This protein is a specific protein that is encoded in the nerve cells. In this study, the major section under consideration was the characteristics of the differentiation process of the P19 cells. In specific, the acquisition of a neuronal phenotype was evaluated by expressing the microtubule-associated protein 2 (map-2) as a dendritic indicator in order to identify axon. The cells that were marked using MAP-2 antibodies were visible when seen under the microscope, as is demonstrated in Fig.6 In this figure, a positive reaction between green phosphorous areas and their respective antibodies was observed due to the presence of MAP-2 proteins. Since this protein represents neuronal cells, its presence confirms successful differentiation of P19 cells into neurons following the culturing process. Furthermore, the tubular morphology provided by the method for separating the phase is a proper structure for the growth and penetration of the neural cells.[18] Fig. 6. Fluorescence imaging of the cells marked with Map-2 antibody on the scaffold after 14 days of culturing, a) control, b) 5% gelatin/10% PVA in -196° Overall, the suitability of the obtained scaffolds for adhesion, differentiation, and cellular aggregation of P19 cells into nerve cells is confirmed using the immunofluorescence and the cell-culture experiments. As can be seen in the results obtained, the technique proposed in this paper is an excellent method for the construction and fabrication of scaffolds. This technique can also be utilized for applications in neuron repair. Furthermore, it facilitates porous, free-standing and flexible 3D fabrication to support neural and glial cell growth, adhesion, and differentiation for up to two weeks.

Conclusion: 4. Conclusion In this study, morphological examinations were carried out using images from the scaffolds obtained using a scanning electron microscope (SEM). The gelatin scaffold’s inner structure along with the difference in the size of the pores demonstrated the differences in the ratio of heat transfer during the

scaffold's freezing. The number of nuclei of the crystallization of ice may be fewer at higher freezing temperatures, which increases the final size of the crystals. Since larger crystals tend to expand the gelatin chains, the scaffold's pore size will increase, leading to the destruction of the structure. On the other hand, rapid cooling may form many nuclei of ice crystals and create pores with smaller size. The fast freezing procedure in N2 (l) for a duration of 20 minutes created sponges that have smaller pores (compared to what was obtained through a slow freezing process that is carried out in a freezer and includes maintaining in -4°C for 24 hours). In other words, the difference in the pores' inner structure and their size demonstrates the differences in the ratio of heat transfer while the swollen scaffolds are being frozen. Hence, a sufficiently high cooling ratio, as in N2 (l), will be capable of extracting the crystallization heat and thus, preventing the formation of larger crystals of ice. Finally, frozen substances are dried by subliming the crystals of ice under vacuum at a temperature lower than the freezing temperature. Therefore, the freeze-dried scaffolds pore size can be exclusively controlled using the size of the crystals of ice formed in the freezing process. Formation of larger porous structures that have brittle and walls with more rapture is probably the result of larger crystals of ice that formed at lower freezing ratios. On the other hand, the N2 (l) cooling process yields a larger number of crystals of ice with smaller sizes. In this study, similar effects of the ratio of freezing on the mechanism in which scaffold's porous microstructure was formed were studied. The temperature in which freezing occurred is effective in the freeze-dried scaffold's inner structure through constructing channels, as shown in Fig. 5. In these channels, the direction is most likely identical to the direction of the formation of the crystals of ice. If the ice is formed with no external force, the crystals will most likely form randomly with no dominant direction. However, in the presence of an external stress, e.g. rapid cooling, crystals are oriented according to a temperature gradient that is induced in the gelatin scaffold.[12] Providing priority over the channel pores' alignment may provide exceptional advantages in certain applications in medical engineering, including nerve regeneration. In order to provide sufficient space for extracellular matrix production and growth of the cells, most scaffolds employed in tissue engineering are highly porous. Regarding this point of view in tissue regeneration, the proposed method provides a desirable method to obtain biodegradable scaffolds that have interconnected pores to be utilized in mass diffusion control. L-929 fibroblast cells, mediated by the MTT test, were utilized to determine the scaffold's suitability and interaction of cells. According to in vitro analysis, a significant increase in the metabolic activity was observed in contrast with the control, which resulted in the differentiation of the P19 cells over the surface of the scaffold. Through employing biocompatible procedure, a highly consistent, interrelated, and viable neural network was formed on scaffolds over a course of 14 days. Adapting these scaffolds to the necessary roughness and architecture requires a more comprehensive study on P19 cells' growth control, along with predicting the potential applications of these substances in the construction of neural repairers.

Keywords: neural tissue engineering, gelatin, PVA, laminin.

PREPARATION AND CHARACTERIZATION OF HIGHLY POROUS NANOCLAYENRICHED POLY (Ɛ-CAPROLACTONE) SCAFFOLDS AND EVALUATION OF OSTEOGENIC DIFFERENTIATION OF HUMAN MESENCHYMAL STEM CELLS (Research Paper)

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Introduction: Introduction: In the last decades, tissue engineering has an effective role in introducing osteo Bioimplants1.Co-cell polymer with nano-clay can be one of the best implants for taking the place of bone failing and defecting in patients2,3. Human mesenchymal stem cells (hMSCs) and nano clay polymeric scaffolds can be biocompatible and biodegradable in the body4. The nano clay_enriched polycaprolactone (PCL) scaffolds aid hMSCs proliferation and adhesion 5. Layered double hydroxide (LDH) nano clay can improve PCL properties in stem cellsdifferentiation3. Therefore the aim of this study is to fabricate bio-active and bio-interactive highly porous(more than 94%) PCL scaffolds composited with different amounts of LDH at low temperatures.

Methods: In this study, highly porous PCL scaffold doped with different contents of LDH (ranging from 0.1 wt.% to 10 wt.%) simultaneously and the LDH attended smoothly dispersed throughout the PCL scaffold as confirmed by energy dispersive X_ray analysis (EDX). The viability, proliferation, morphology, attachment, and osteogenic differentiation of hMScs were assessed, and also mechanical behavior, degradation, and porosity of scaffold were examined. The osteo genes expression did for confirmation osteogenic differentiation of hMSCs.

Results: This nanocomposite scaffold containing 1wt% of LDH_enriched PCL showed more excellent mechanical properties compared to that pure PCL. The presence of LDH in polymeric scaffold promoted in vitro bio-mineralization and osteogenic differentiation. Experimental tests demonstrated that highly porous scaffold has no toxicity on the cells and also causes cell adhesion and proliferation.

Conclusion: These results demonstrated that the addition of LDH improved the osteogenic differentiation while compression strength, hydrophilicity, and degradation rate were also increased. Overall this nanocomposite scaffold could be a suitable candidate for bone tissue engineering scaffold applications.

Keywords: Keywords: layered double hydroxide, polycaprolactone, nano clay, bone tissue engineering

preparation and characterization of noscapine loaded superparamagnetic iron oxide nanoparticles for drug delivery in breast cancer cells (Research Paper)

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Introduction: Despite encouraging progress in cancer diagnosis and therapeutic strategies, breast cancer remains the primary cause of cancer-related death among females (1). Superparamagnetic iron oxide nanoparticles (SPIONs) are pharmaceutically attractive drug carriers due to their biocompatibility, biodegradability, facility tunable, and feasibility to synthesize (2,3). This study aimed to deliver noscapine (an opium alkaloid) to metastatic breast cancer cells by the aid of SPIONs.

Methods: Fe3O4 SPIONs were first prepared by the co-precipitation method. The SPION-chitosan–drug nanoparticles were prepared by the ionic gelation technique. XRD, FTIR, DLS, TEM, and spectrophotometry were used to characterize the drug system. MTT assay was used to assess the cytotoxicity on 4T1 triple-negative breast cancer cell.

Results: The complex with the highest drug loading rate of about 96% and an average particle size of 419 and 20 nm (DLS and TEM, respectively) was considered for further evaluation. The XRD results were indicated typical diffraction patterns of magnetite nanoparticles. Our result showed that noscapine and noscapine-magnetic nanoparticles (MNP) abolished 4T1 proliferation dose-dependently with an IC50 value of 127.7 and 697.8 µg/mL respectively, whereas, SPION and SPION-chitosan were found to have no cytotoxicity.

Conclusion: Contrary to papaveine-MNP, the other opium alkaloid, that has prepared by the aforementioned method and demonstrated a potent inhibitory activity (IC50: 11.5 vs 62.4 µg/mL for papverine), noscapine-MNP was not efficient for drug delivery.

Keywords: Magnetic nanoparticle, Noscapine, Papaverine, Breast cancer, Drug delivery

Preparation and characterization of the bilayer nanoparticles of nonionic surfactant encapsulated buniun persicum (Research Paper)

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Introduction: Niosomes are colloidal particles formed from the self-assembly of non-ionic surfactants in aqueous medium resulting in closed bilayer structures. As a consequence of this hydrophilic and hydrophobic structure, niosomes have the capacity to entrap compounds of different solubilities. Niosomes are promising vehicle for drug delivery which protect sensitive drugs and improve the therapeutic index of drugs by restricting their action to target cells.

Methods: Essential oils are complex mixtures of volatile compounds such as terpenoids, phenol-derived aromatic components that have been used for many biological properties including bactericidal, fungicidal, insecticidal, antioxidant, anti-tyrosinase and other medicinal properties. Encapsulation of essential oils in niosomes can be an attractive method to overcome their limitation such as volatility, easily decomposition by heat, humidity, light, or oxygen. buniun persicum is an aromatic plant included in the Apiaceae family and is used to flavor foods, added to fragrances, and for medical preparations.

Results: The major components of the Cumin oil were reported as cuminaldehyde, γ -terpinene, Kvmynaldyyd , Limonene , 1v 8- Cineole, Terpinene-7-al, and paracymene, paramentha-1,3din-7al which provide the antimicrobial and antioxidant activity. The aim of this work was to formulate Cumin essential oil-loaded niosomes to improve water solubility of natural product and evaluate its physico-chemical features and stability.

Conclusion: Cumin oil was obtained through steam distillation using a clevenger-type apparatus and GC/MS was applied to identify the main components of the essential oil. Niosomes were prepared by using thin film hydration method and nanoparticles were characterized for particle size, dispersity index, zeta potential, encapsulation efficiency, in vitro release, and morphology.

Keywords: buniun persicum , Cumin, Niosome, Essential oil, encapsulation.

Preparation of chitosan hydrogels containing spirulina and glutathione extract for use as anti-inflammatory skin care (Research Paper)

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3.

Introduction: Spirulina, a seaweed which is a blue-green algae biomass, belongs to the class of cyanobacteria discovered by non-referenced Mexicans in the 16th century and has been used as a daily food source. It is enriched with lots of vitamins, nutrients, antioxidants, proteins, pigments, minerals and is considered a wonder of nature. Free radical-induced oxidative damage has long been thought to be the most important consequence of the aging process. In this project the Spirulina extract and Glutathione were used in Chitosan hydrogel preparation. The cytotoxicity and proliferation effects of chitosan nanohydrogels containing Spirulina extracts and Glutathione by MTT assay. Moreover, migration of HFF-1 cells was evaluated by Scratch test. The expression of important genes in skin rehabilitation were assessed by Real Time PCR.

Methods: The physicochemical characterization of Nanohydrogel was evaluated by DLS and TEM. The interaction between functional groups of TPP and Chitosan by FT-IR. The cytotoxicity effect of nanohydrogels was assayed by MTT in different time points 24, 48 and 72 hours. The migration assay was done be scratch test furthermore the main gene (TGFβ, TNFα) expression in skin rehabilitation were analyzed by Real Time PCR. Statistical analysis was done by Graphpad Prism v.8 and ONE-WAY ANOVA and T-Test analysis.

Results: The results showed the significant effects of Chitosan hydrogels containing Spirulina extract and Glutathione on cell proliferation and migration assay. More than two folds of proliferation rate was confirmed after 48 hours incubation. The expression of genes was significantly increased after 24 hours incubation. The migration effects of hydrogel were qualitatively evaluated by scratch test. The different of migration was seen among different kinds of group treatments. The best results were achieved in treated cells by chitosan nano hydrogels containing Spirulina aqua extract and Glutathione.

Conclusion: In this project the functional effects of nanohydrogels were confirmed in cellular and molecular levels.

Keywords: Spirulina, Glutathione, Chitosan hydrogels, anti-inflammatory, Skin rehabilitation

Presence and expression of human papillomaviruses in two cell lines of reproductive origin (Research Paper)

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Introduction: Human papillomaviruses (HPVs) are responsible for a number of anogenital and head and neck cancers. HPV DNA has been present and transcribed in most cell lines established from human cervical carcinomas. The aim of this study was to elucidate whether two cell lines of the reproductive system including normal cervical cells and an ovarian cell line express HPV.

Methods: HNCF-PI 52 cells originating from the primary culture of a healthy female uterine cervix and a human ovarian carcinoma cell line (A2780) were both tested for contamination with HPV. DNA and RNA extraction, cDNA synthesis, and PCR amplification using two sets of CP and GP primers were used.

Results: Results from the nested PCR reaction of degenerate primers of CP together with PCR using GP primers show that HNCF-PI 52 express HPV. No HPV DNA was detected in the A2780 cell line.

Conclusion: In basic biological research, cell lines of reproductive origin are frequently used by scientists or in the diagnostic laboratories. The finding of this study reveals that HPV is present and express in a normal cervix tissue cell line.

Keywords: Cell culture, Viral contamination, Human papillomavirus (HPV), HNCF-PI 52, A2780

Presentation method to inference and interpretation of copy number changes and genomic rearrangements breakpoints in single-cell sequencing of ovarian cancer (Research Paper)

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Introduction: Novel cancer genomics has emerged from the combination of the Human Genome Reference, massively parallel sequencing, and the measurement of tumor to normal DNA sequences, revealing novel insights into the cancer genome and its amazing diversity. Whole genome sequencing mixes the signals of sampled populations, diluting the signals of clone-specific aberrations, and complicating estimation of clone-specific genotypes.

Methods: We introduce ReMixT, a method to unmix tumor and contaminating normal signals and jointly predict mixture proportions, clone-specific segment copy number, and clone specificity of breakpoints.

Results: We have demonstrated that ReMixT improves both inference and interpretation of copy number changes and genomic rearrangements. Improved accuracy was observed for prediction of clone fraction, clone specific copy number, and clone specificity of breakpoints. We show how breakpoint copy number changes can be used a markers of clonal populations, and used to track clonal population dynamics in the same way as SNVs.

Conclusion: By linking clone specific copy number changes to breakpoints we show how targeted single cell sequencing can be used to jointly profile clonal genotypes in SNV and copy number space. We anticipate further benefit may be gained from jointly modelling copy number changes, rearrangements, SNPs and SNVs, all within the context of an appropriate phylogenetic model. Future research leveraging the patterns of genome damage and the totality of somatic alterations in a cancer's evolutionary history to elucidate its biologic and mutagenic properties will derive benefit from ReMiXT's improved accuracy in structural alteration detection and interpretation.

Keywords: Whole genome, Cancer genomics, SNV, SNP, ReMixT

Prevalence of Von Willebrand Disease in Women of Reproductive Age with Heavy Menstrual Bleeding in Kashan, Iran During 2019 (Research Paper)

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Introduction: Von Willebrand disease (VWD) is an inherited disorder of blood clotting in humans. The prevalence of VWD is different among various populations. Prevalence of this disorder in women with menorrhagia is less reported in Asia and Iran. The present study was aimed to determine the prevalence of VWD in women of reproductive age with Heavy Menstrual Bleeding.

Methods: In this cross-sectional study, 160 women in the reproductive age group (15-45 years) with Heavy Menstrual Bleeding (HMB) referred to the Hematology Clinic of Kashan Shahid-Beheshti Hospital during 2019 were participated. Demographic characteristics, clinical testing and physician reported problems of each participate including age, menstrual intervals, having the uterine myoma and polyp were collected using a questionnaire, sonography and physical examination of women by a physician. The laboratory tests included hemoglobin (Hb), ferritin, Iron and total iron-binding capacity (TIBC).

Results: Fifteen patients (9.3%) with severe menstrual bleeding had VWD with the mean age of 34.60±6.85 years. Frequency of the uterine fibroid (Myoma) in women with VWD was significantly more than its rate in patients without VWD (p=0.03). The mean of ferritin among 15 women with and 145 women without VWD was 23±4.28 ug/dL and 30.68±4.46 ug/dL, respectively (P=0.001). The average of serum iron in total participants was 35.3±11.48 ug/dL and VWD patients had a lower iron than those without VWD (P=0.001). There was not a significant difference in TIBC level between women with and without VWD (P=0.6).

Conclusion: VWD accounted for 9.3% of women of reproductive age with heavy menstrual bleeding in Kashan, Iran, which is lower than other regions of Asia.

Keywords: Prevalence, Menorrhagia, Von Willebrand Disease

prevent the birth of people with Down syndrome (Review)

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Introduction: Down syndrome is a genetic condition caused by an extra copy of genetic material from a complete or even partial chromosome 21. Down syndrome is not a disease but a set of features that result from this change. This extra chromosome can affect a person's body, intelligence, overall growth, and increase the risk of some health problems. Each cell in the body contains genes that are located in the nucleus of a cell in the form of a chromosome. There are 46 chromosomes in each cell, 23 of which are inherited from the father and 23 from the mother. When some or all of a person's cells contain an extra copy of chromosome 21, Down syndrome develops. People with Down syndrome have upward-pointing eyes with diagonal seams, skin folds in the inner corners and white spots on the iris, low muscle tone, short stature and neck, smooth bridge of the nose, single and deep lines in the middle of the palm, The tongue protrudes from the mouth, there is a large space between the big toe and the second toe and the curvature of the fifth toe inside. Symptoms of Down syndrome include growth retardation; Children with the syndrome often reach significant stages of development after the same age. They may open their mouths late and need speech therapy. In these children, fine motor skills may be delayed, they may need some time to acquire major motor skills, and they may have difficulty concentrating and paying attention. A child with Down syndrome averages; She is 11 months old At 17 months, he has four limbs She is 26 months old About half of children with this syndrome have congenital heart defects and have respiratory problems, hearing problems, Alzheimer's disease, childhood leukemia, epilepsy, and thyroid disorders. Women whose children are more likely to develop the syndrome are screened, and women between the ages of 30 and 35 are screened during pregnancy. Screening tests include: Nuchal translucency testing Triple screen or quadruple screen Integrated screen _Cell-free DNA testing Genetic ultrasound Screening is a low-risk way to determine if advanced diagnostic tests are being performed Diagnostic tests for Down syndrome and other problems are more accurate. These tests are usually done on the uterus and increase the risk of miscarriage or premature birth. Sampling of pair feathers Amniocentesis - Subcutaneous blood sampling of umbilical cord blood After the baby is born, Down's syndrome can be diagnosed by examining his or her physical characteristics as well as his or her blood and tissues. There is no specific treatment for Down syndrome, and people with this syndrome, like others, receive medical care.

Methods: By review other article

Results: As it is known, this syndrome is more common in the children of women between the ages of 30 and 35 or older, who can prevent this syndrome by taking the necessary tests before pregnancy.

Conclusion: Pregnancy can be prevented by screening and other tests. Therefore, it is best to get pregnant at an early age to eliminate the risk of their child developing Down syndrome.

Keywords: Down Syndrome, Symptoms, Prevention, Chromosome 21, Screening

Prevention and Diagnosis of Quaid 19 (Review)

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Introduction: Coronaviruses are a large family of viruses and subordinate viruses that range from the common cold virus to more serious diseases such as SARS, Morse, and Covid 19. Their structure also has a typical Aranian genome. The structure of this virus consists of two layers; The nucleus of the virus is made up of genetic material and the outer layer is made up of protein crowns. After entering the host cell, the virus particle is uncovered and its genome enters the cell's cytoplasm. Coronavirus is a new type of infectious disease caused by the recently discovered coronavirus. How is coronavirus diagnosed? 1 polymerase chain reaction (shows if you now have corona) 2 antibody tests or serological tests (shows if you have had coronavirus in the past) Polymerase chain reaction In the first half of January, Chinese researchers identified the genetic formula for the coronavirus and made it available to all. For this, a suspected person with a sore throat or nose will be sampled and sent to a laboratory Samples are usually taken from people who have a fever, shortness of breath, and a cough. To diagnose this method, quantitatively, an enzyme called reverse transcriptase is used, which makes it possible to determine the number of viruses from the number of genomes in the tested sample in addition to detecting the virus. The reverse transcriptase enzyme is obtained using part of a single-stranded virus genome, followed by a double-stranded version of the supplement, or DNA, and then the genetic content is multiplied using a chain reaction, followed by fluorescence. And a method called the amount and type of genetic material of the virus is determined at the moment. Coronavirus testing is done in 3 steps To diagnose coronavirus, the test is first performed to identify it, and then the result is confirmed by another test, if both tests are positive; The third test determines the type of coronavirus. In the field of coronavirus detection, by performing the necessary tests, it is determined between 24 and 72 hours whether the person is infected with this virus or not. Anti-wind test: Some blood will be taken from you and the following two chemicals will be checked in your blood: IgM antibodies, which are formed early in the infection. IgG antibodies, which appear later in the body after recovery. It takes about 4 weeks for IgM antibodies to form in the human body Antibodies can show the prevalence of covid 19. Researchers are studying how to extract plasma from patients with improved antibodies and use it to treat patients with covid 19. Coronavirus prevention: There is currently no specific vaccine for Corona 2019. Avoid close contact with sick people Avoid touching your eyes, nose or mouth Stay home when you are sick Clean and disinfect objects and surfaces you are dealing with. Wash your hands with soap and water several times a day for at least 20 seconds. Drugs that affect coronavirus: Drugs that affect viruses in a way that stops the growth and activity of the coronavirus inside the body. Drugs that can calm the immune system. Nowadays, people with the coronavirus become worse when their immune system reacts too much and damages the main organs of the body. Antibodies obtained from the blood of infected patients or made in a laboratory capable of attacking the virus

Methods: by review other article

Results: The best way to prevent this disease is to wash your hands and reduce contact with other people

Conclusion: So far no cure has been found for this virus, so the treatment of this virus includes care and prevention. For this purpose, if you have this virus, you should rest and use acetaminophen and ibuprofen to reduce pain and fever.

Keywords: Quaid-19, Prevention, Treatment, Diagnosis

Prevention of cervical cancer (Review)

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Introduction: in general, a disease that begins with the abnormal proliferation of normal cells in the body is called cancer. Cervical cancer is a type of cancer that occurs in cells in the lower part of the uterus that connects to the vagina, and when cervical cells grow abnormally and multiply rapidly, cervical cancer occurs. About half a million women with the disease are diagnosed worldwide each year, the main cause of which is a specific type of virus called human papilloma, which has more than 200 strains, only some of which cause non-cellular. Normal in the cervix HPV is transmitted through sexual intercourse Other causes of the disease include smoking, having multiple sexual partners, premature sexual activity, weakened immune systems, and long-term use of birth control pills. Cervical cancer begins at age 25 and peaks at age 47. And one in 128 women has cervical cancer, one of the symptoms of which is bleeding that occurs during regular menstruation. Bleeding after sexual contact or vaginal lavage or pelvic exam. Prolonged menstrual bleeding or more severe than usual. Note that there is bleeding after menopause One way to diagnose cervical cancer is to have a Pap smear. The doctor sends a tube through the vagina into the patient's genitals and samples are taken from the cervical cells. This sample is taken by a pathologist in terms of cancer cells and Abnormalities and HPV are examined under a microscope. The best time to do the test is two weeks after menstruation and 48 hours after intercourse. Another method is to examine the cervix. The doctor examines it with a device called a colposcope. He was diagnosed with cervical cancer, HPV vaccination and having safe sex and not having sex at an early age.

Methods: The following article is an overview of the keywords Search for Cancer, Cervical Cancer, Pregnancy, Pop Smear in Google Search Engine and sid database, and uses 8 article

Results: According to the introduction, having safe sex, using a condom, having fewer sexual partners, delaying sex, and getting the HPV vaccine are the most important things in preventing and reducing the risk of developing and dying from uterine cancer. Get acquainted (gain, obtain) with present-day techniques that came from Screenplay and Pap smear, which are not only preventable but also detect abnormal changes in the early stages by removing and killing altered cells before the cell. Cancer can prevent cancer from progressing

Conclusion: Therefore, by providing appropriate training on how to have safe sex education and reminders of the need for Pap smear testing and personal hygiene, it can have a significant impact on preventing and reducing the risk of cervical cancer and mortality.

Keywords: cancer،cervical cancer،prevention,Pap smear

Prevention of food allergic in infants and children (Systematic review) (Review)

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Introduction: Food allergies occur in children and infants for different reasons in the world. In addition to genetics, food is another factor for development of allergies. Understanding the impact of food and environmental factors is the most important issue because food allergies in the early years of life lead to allergies in later life

Methods: This systematic review article was performed within articles published at PubMed, Scopus, Google Scholar, SID and web of science from 2010 to 2020. The keywords were "Prevention", "food allergic", "infants" and "children". The articles were chosen from Persian and English. 170 articles were found, and the search protocol was limited to access the full text and last ten years, it was limited to 154 articles, and a number of them by reading titles were removed.

Results: Finally, 120 studies were conducted. In several articles, cow and egg milk allergies were identified as the most common allergies. A number of articles have highlighted the importance of breast milk because breast milk provide needed proteins and vitamins for baby, also it is essential for growth and strengthening of the immune system, they have showed it has very important impact on preventing food allergies. The other articles emphasized on the importance of vitamin D deficiency during infancy and exposure to antibiotics in the first year of life. Some of the studies have investigated food allergies in infancy lead to atopic dermatitis and asthma in childhood.

Conclusion: Premature and breastfed infants are at higher risk for food allergies than adults. Therefore, vitamin D deficiency and exposure to antibiotics could maximize the risk of allergies. This seems that breastfeeding would prevent allergies in infants if mother's diet and her immune system improved.

Keywords: Prevention, Food allergy, Children, infants

Prevention of gynecological diseases for fertility (Review)

Mahya Badbarouni,[1,*]

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Introduction: When it comes to sex between men and women, we need to be careful about the concept of health, because death is more vulnerable among women than men.Research shows that insufficient awareness and non-observance of proper health behaviors in any society is inevitable. People and communities in Burley need to know how to live the right way of life and stay healthy, and to avoid getting sick. They need to be taught the right health behaviorsWhich is possible through schools from childhood. One of the women's diseases that causes infertility and serious problems in women and endangers their health includes urinary tract infections and vaginal infections. Some secretions in women and girls are normal, and based on the color and smell of the discharge, it can be determined whether the discharge is normal or infecti. Knowing some of the features, it can be said that the secretion is abnormal. Natural secretions are necessary for the health of the vagina, which is caused by the activity of a series of beneficial and non-pathogenic bacteria that prevent fungal and bacterial infections. The natural secretions are clear, white, colorless, odorless, thick, or thick, and do not cause burning or itching. Some women's infections are marked by itching, burning, and discoloration in the discharge and have a foul odor. Women's infections include fungal infections, bacterial infections, parasitic infections, and urinary tract infections. Here are some simple tips to prevent women's infectious diseases: 1. Clean yourself from front to back after urination to prevent anal bacteria from being pushed into the vagina. During the day, wear cotton underwear and avoid wearing nylon underwear at night when resting. Avoid wearing tight clothing such as jeans and make-up for a long time. Use non-scented detergents to wash underwear.Do not use hot tub. Change your underwear at least once every two days. Be sure to urinate before having sex. Change the sanitary napkin between four and six hours, or a maximum of eight hours, and wash your hands with soap and water before using another sanitary pad. Do not use sanitary napkins or scented wipes. Replace your wet underwear quickly. Avoid overuse of antibiotics that kill the beneficial bacteria in the vagina. The use of birth control pills that alter hormones, and during pregnancy and lactation, should be more careful about women's infections and health. Side effects of delayed treatment of gynecological infections and incomplete treatment include: Infertility, ectopic pregnancy, chronic pelvic pain, abscesses, and clogged fallopian tubes. And adhesions that cause the uterus to rupture the ovaries or tubes. These female infections lead to premature birth or low birth weight babies.

Methods: by reveiw other article and book

Results: In some parts of the world, there are still deprived areas that, due to economic poverty or lack of knowledge, ignore the necessary training to prevent women from contracting infectious diseases. Simple things like female infections are found.

Conclusion: By following a series of simple health tips, women's infectious diseases can be easily prevented and infertility can be easily reduced

Keywords: Female infections, fertility, health

Prevention of HIV transmission through breastfeeding (Review)

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Introduction: Acquired immunodeficiency syndrome (AIDS) is a disease caused by the human immunodeficiency virus (HIV). The majority of childhood infections are acquired through mother-to-child transmission (MTCT) during pregnancy, labor, delivery, and breastfeeding. Prevention of mother to child transmission (PMTCT) through breastfeeding by effective strategies is an important subject in debates. We summarized the strategies shown to have efficacy on PMTCT through breastfeeding.

Methods: The literature search was performed using the Pubmed, Google Scholar, and Science direct databases between 2010 to 2020 by the combination of terms: " prevention", "breastfeeding" and "HIV" as keywords. In all 64 results, 10 related articles were selected. Duplicate and unrelated cases that discussed other issues were excluded.

Results: 1. It was recommended that mothers living with HIV should breastfeed for at least 12 months while maternal combination antiretroviral therapy (cART) and prophylaxis for infants are provided during the whole duration of breastfeeding. 2. It was shown that exclusive breastfeeding during the first six months is associated with a lower risk of MTCT than mixed feeding. 3. It was recommended that maternal ART and infant prophylaxis should be continued until one week after breastfeeding ends. 4. Extended once-daily infant nevirapine up to 6 months was shown to be safe and led to a 54% reduction in MTCT of HIV-1 via breastfeeding. 5. It was demonstrated that triple antiretroviral prophylaxis (based on zidovudine, lamivudine, and lopinavir/ritonavir) was more efficient than a short prophylaxis regimen of zidovudine and single-dose nevirapine (NVP) in infected mothers. 6. It was recommended that Mothers should stop Breastfeeding gradually within one month. Abrupt weaning is associated with elevations in viral load in breast milk. 7. It was reported that the use of alkyl sulfate microbicides such as 0.1% SDS may be a choice to help inactivation of HIV-1 in breast milk. 8. Heat treatments such as Holder pasteurization, Pretoria pasteurization, and "flash-heat" treatments were shown to be a good practice eradicating HIV-1 from breast milk.

Conclusion: Improvement in PMTCT during breastfeeding is achieved by using appropriate and effective strategies for both HIV-infected mothers and their breastfed infants.

Keywords: prevention, breastfeeding, HIV

probiotics and colorectal cancer (Review)

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Introduction: The human body contains more than 100 trillion microbes, most of which are hosted in the gut, although there are different communities residing in a vast range of body niches. This population is called the microbiome and comprises a wide variety of microorganisms, including archaea, viruses and fungi, although anaerobic bacteria is the most studied group since they are the most abundant. These microbial communities are acquired at birth and are essential for maintaining body homeostasis. The interaction between the host and the microbiome is dynamic and controlled by a huge number of genetic and environmental factors, such as age, geography, alcohol or drug intake and diet. although intestinal microbiota have been shown to be individual and variable over time, only two predominant phyla, namely Firmicutes and Bacteroidetes, comprise over 90% of all endogenous bacteria present in healthy adults. Other members of the normal colonic microbiome include Eubacterium, Bifidobacterium, Fusobacterium, Lactobacilli, Enterococci, Streptococci or Enterobacteriaceae.

Methods: Dysbiosis and Colorectal Cancer: Breaking the Mutualism Although it is not yet clear how dysbiosis could induce colonic carcinogenesis, chronic inflammation appears to be the main mechanism. This hypothesis is supported by the fact that many types of cancer are caused by chronic inflammation. For example, inflammatory bowel diseases (IBD) are linked to an increased risk of colon cancer. The first stages of these diseases involve an alteration to the normal flora, which results in activation of the immune system, thus giving rise to the inflammation that characterizes IBD. As IBD patients have a higher probability of suffering CRC, and dysbiosis has been observed in some cases, it is possible to assume that IBD-related CRC is driven by a previous dysbiosis stage. As a result, the microbiome has started to be considered one of the prime suspects responsible for the onset and/or evolution of colonic carcinogenesis. This research field is based on the differences found in microbial signature between CRC patients and healthy populations. Indeed, next-generation sequencing methods based on 16s rRNA have revealed an enrichment in proinflammatory bacteria, such as Fusobacterium, which is also overrepresented in other diseases (for example IBD), as well as a lower abundance of butyrate producers, such as protective bifidobacteria.

Results: Potential mechanisms of probiotic action in CRC chemoprevention Adhesion of probiotics and competitive exclusion of pathogenic intestinal flora Alteration of intestinal microflora enzyme activity Reduction of carcinogenic secondary bile acids Binding of carcinogens and mutagens Chemopreventive role of short chain fatty acids

Conclusion: In conclusion, there is a convincing body of evidence suggesting various potential mechanisms of action of probiotics in CRC prevention. It is clear that the chemopreventive effects of probiotics are dependent on the strain of the

microorganism. Emerging data suggest viability may not be a prerequisite for probiotics to exert its anti-CRC activity. Synbiotics is likely to be more effective than either prebiotics or probiotics alone, as indicated by the growing body of data. More in vivo, especially human studies are warranted to further elucidate and confirm the potential chemopreventive role of probiotics (viable and non-viable), prebiotics and synbiotics in CRC.

Keywords: Probiotics; Colon; colorectal carcinoma; microbiota; cancer

Promote agricultural style of Halophytes In the lands of Urmia Lake to stabilize fine dust and prevention disease (Review)

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Introduction: Urmia lake is a lake in northwest of Iran which is located between the two provinces of eastern and eastern Azerbaijan and is the sixth Salt Lake in the world. The lake is highly saline and is mostly fed by Zarrineh River, Simineh River, Talkheh River, Gader, Baranduz, Nazlu and Zola rivers. Since the mid - 1980 s, the lake has begun to dry and is now at risk of being frozen, including the land - on - lake highway, intensive use of catchment sources, non - expert agriculture regardless of the area " s culture capacity, construction of numerous dams and for natural causes, reduction of snow and rain and drought. The report suggests that by 2015 the lake has lost 88 % of its area; however, in recent years, such as elsewhere in Iran, it has seen torrential rains in the spring that contributed to the revival of part of the lake. experts compare the condition of the Urmia lake with the Aral Sea in the central Asian region. The Aral Sea, which was located in Russia (former Soviet Union), was a vast, salty lake that gradually dry up and disappeared due to the diversion of its flowing rivers. After drying up, there were many salt storms that caused various illnesses, including reducing the sight of people in the region, high blood pressure, severe anemia in teenagers and pregnant women, or birth of premature babies or physical and physical disabilities unfortunately, we have witnessed the occurrence of this phenomenon in Urmia lake as time has been repeated. The study suggests that it has been enhanced by the drying of the lake, blood and skin infections that reflect the harmful effects of light. some environmental pundits predict that the temperate climate of the region will be converted into tropical climates, and the environmental conditions in the region will be changed. In addition to salt, many contaminants, including heavy toxic metals used in agriculture, penetrate into the surface and subsurface waters associated with the lake, and many of the toxic substances are aerobic when the lake is completely dry The most important cause of destructive environmental effects and disease in the inhabitants of the dried lakes is toxic dust that rises into the air due to sediments deposited on the shores of the lake. Dust is one of the effective geological factors in causing diseases and has different pathogenic potentials depending on the particle size, intensity and duration of contact between the combination of mineralogy and associated pathogenic microorganisms. In addition, the dust - dust phenomenon is causing damage to the agricultural sector, which includes the decline in agricultural soil fertility and the introduction of toxic compounds to the food chain, including those. In addition to the occurrence of dust, the dust of the salt and soil particles on the leaves and stems, and the possibility of proper use by animals is eliminated. When livestock are forced to feed on fodder, it will be inevitable to cause numerous digestive problems and metabolic diseases. predicted by the drying of the lake, we have witnessed heavy rainfall in many neighboring provinces, which will lead to more than 13 m people displaced. This displacement will eventually lead to mass migration of people to cities and eventually to other countries as well as to other continents, which in turn will have irreparable consequences for the whole world. Although the name of the dried lakes

has been associated with the creation of dust hotspots, it should be borne in mind that in recent years human knowledge has been able to largely control this crisis; For example, measures taken on Lake Owens in the United States show that the use of methods such as identifying dust production centers, using dust collecting filters and studying the chemical elements in the particles has been effective in adopting appropriate methods to control fine dust. These studies have been done to some extent in Lake Urmia. Therefore, studies will not harm the ecosystem of the region by increasing vegetation to control dust, nor will there be any problems if Lake Urmia is rehabilitated. Plants that can grow in the soils around Lake Urmia must first of all have an important common feature and that is soil salinity tolerance, i.e they are among the halophyte (salinity) plants. Agriculture Salinity is the exploitation of saline water and soil resources for the production of crops and horticultural products, both saline and non-saline. Salinization is an economic technology of exploitation of unusable saline water and soil resources in conventional agriculture with emphasis on environmental aspects. (Dehghani et al., 2016) Saline plants are plants that are able to complete their life cycle in saline soils. Saline plants (or saline plants) are plants that can coexist with seawater and other water and saline soils and reduce excess salt in the soil. Seawater can also be used to irrigate them. Due to the rich resources of sea water, these plants are a great help to control desertification and desertification. Several countries use these plants in their ecosystems. Approximately 11.1% of the earth's plant flora is composed of salinity-resistant salts. Saline products can even be used as fodder, wood, medicinal and oily plants, cover and ornamental plants, bio-drainage, bioremediation of detergents, dyeing and tanning, windbreaks, ecosystem stabilization, biofuel production, etc. Also, with salinity agriculture, the pressure on fresh water resources is reduced (Kafi et al., 2011) Genetically, saline plants are plants that can grow and produce in saline soils due to their specific gene sequences. By studying gene sequences, it was found that one of the genes that can give this property to plants is the DREB gene. Among halophyte plants, Salicornia plant, having DREB gene, has been considered for producing oil, livestock fodder and edible vegetables using lake water and cultivation power in saline soils. The natural habitat of this plant is salt flats, sea shores, swamps and salt marshes of Europe, South Asia, North America and South Africa (Singh et al., 2014) There are many plants in the category of halophytes that can be used for various purposes such as food and agriculture or ornamental and creating green space due to their resistance and adaptation to the climate of the region. Atriplex Spp, which is an evergreen plant, belongs to the group of saline plants; And sea water can be used to irrigate it. Properly covered, it will withstand a great deal of adverse conditions in the summer and fall, when most plants die. Sometimes, the amount of vitamin A in this plant per gram, even more than 35 mg. The roots of this plant are straight and deep, so that sometimes it reaches a depth of four meters. The foliage of this plant, with its large expansion, becomes a shrub and prevents the flow of water in it for areas that have salty soils and about 200 mm per year, rainfall is possible from 3 to 4 months. Therefore, these plants are effective plants for desertification. It is resistant to cold and heat, and tolerance ranges between 15 and 40 ° C, and in most parts of Iran, there is a limit. Salicornia is a succulent, succulent, annual plant of the family Chenopodiace and the genus Salicornioideae. The embryo is located in a circular seed or horseshoe and the flowers are complete, the inflorescence is spike and the stem is banded and articulated. So far,

about 60 species of Salicornia have been identified (Ahmadi, Golshan Noor, 2013). One of its famous species is Salicornia bigelovii. (S. bigelovii), which grows in the coastal areas of North and Central America Today, European and Asian countries have paid more attention to this plant, so that its plant is used in European countries for food and in Asian countries for fresh salads and pickles. Salicornia oil is used in medicinal cases (traditional medicine) to treat diseases such as bronchitis, liver swelling, diarrhea, hypoglycemia, anti-inflammatory and cytotoxic activity. Also, this plant has antioxidant and antioxidant properties. Equal to environmental conditions (Isca et al., 2014) So far, Mexico, India, Eritrea, Saudi Arabia and the UAE have successfully cultivated Salicornia Out of 15 species of Salicornia in the world, there are seven species in Iran. Habitats of this plant in Iran include the provinces of Fars, Semnan, Gorgan, Khuzestan, Bushehr, Hormozgan, Yazd, West Azerbaijan, East Azerbaijan, Isfahan, Qom and Tehran. But despite the fact that Iran is one of the main habitats of this plant, studies conducted on this plant in our country are very limited. (Salehi, Dehghani, Ebrahimi, 1396) Recently, this plant has been considered for the development of the southern coastal strip and cultivation in the coastal areas of the Caspian Sea. Here are three main reasons why Salicornia is considered an oily plant: 1-High production potential with sea water Extractable oil comparable to oil of similar plants2- Similar yield to soy with fresh water (Salehi, Dehghani, Ebrahimi, 1396) 3- Salicornia identification studies in Iran show that the Iranian Salicornia species is different from the European Salicornia. Six species of Salicornia have been identified in central and southern Iran. Most species of Iranian Salicornia that are able to tolerate dry conditions are scattered in central Iran, and especially the species Salicornia persica, which needs swampy and saline conditions, is distributed in southern and central Iran

Methods: According to the studies on cultivation of salicornia that has been done in Yazd (Salehi, Dehghani, Ebrahimi, 1396) Salicornia persica was cultivated in this project. Potted soil was planted in different areas in front of this randomly selected lake. The method of cultivation was that after preparing the soil and leveling it properly, the pots were irrigated to harden the soil surface. Then the seeds were poured to a depth of one centimeter of soil in a completely superficial way and covered with stored powder manure. In order not to damage the delicate seeds, this plant should be done completely superficially and fertilization should be done with sensitivity . The soil surface was kept moist until the plant was fully established. After about 20-25 days, the germination stage was observed. Unfortunately, due to the ideal greenhouse or ground conditions for cultivation, and it is not enough to continue the growth of plants, the plant stops growing at the same stage. It is certain that if the cultivation is more specialized and equipped with expert and engineering support, this project can help to change the cultivation method of the region

Results: Findings showed that Salicornia persica grows in soil samples of the shores of Lake Urmia, which is prepared randomly and placed in a pot culture medium. Findings show that this plant is in natural climatic conditions that can be young for a limited period of 20-25 days and is suitable for the soil

Conclusion: Since 1995, the surface of Lake Urmia has decreased in the catchment area due to various reasons such as drought, construction of many dams, construction of Shahid Kalantari road and digging wells that farmers used to irrigate their fields. . The lake caused a change and decrease in the vegetation of the region (Ahmadi et al., 1397) and following the drying of the lake, the saline soil resulting from the drying of the water increased the possibility of salt dust in the air. The release of these dust particles into the air of the region has created many problems on a large scale for the people of the region and perhaps the people of the whole region. Cultivation of annual or perennial plant resistant species is one of the least expensive and least harmful methods . These plants prevent further soil erosion and the spread of these salt dust particles. Considering that the cultivation was done directly in the soil around Lake Urmia, it can be concluded that Salicornia persica has the ability to germinate and grow in this soil and by providing suitable cultivation conditions, it can be grown in saline soils. Areas of Lake Urmia to be cultivated and harvested. In addition to purifying water and soil salinity, saline plants, including salicornia, can be used as a forage and medicinal plant. Therefore, in the future, it can be effective in modifying the ecosystem of West and East Azerbaijan provinces. (Mahsa Taghavi, Laleh Parviz, 1396) According to research, the Salicornia plant, after growing, is placed almost in an umbrella on the soil, and by shading the soil, in case of large-scale cultivation, it prevents further evaporation of soil water. The cultivation of Biglornia salicornia in Yazd has been done successfully and many other species of Salicornia have been cultivated in other countries, but according to the hypothesis, Salicornia persica species, which is native to Iran, can be more successful in the saline soils of Iran and Especially Azerbaijan should be cultivated. Cultivation of salicornia can have many benefits for the region, including: -In addition to its medicinal, ornamental, dyeing and tanning uses, its fodder can be used for animal feed in the region and its oil can be used for human consumption -While preventing soil erosion and prevents the production of salt dust that is caused by salt overflow, it also acts as a wind breaker on the soil surface and prevents the formation of salt storms. -by shading the soil surface in the warm seasons of the year (July and August) prevents further evaporation of soil water and erosion and as a result the production of fine dust. -In case of large-scale cultivation, beautiful landscapes of Salicornia farms will be created in the tourist seasons, which can be helped with proper advertising to the region's tourism, and as in previous years, the presence of Lake Urmia sent a flood of tourists to the region, again. Increased tourism in the region and ultimately helped improve the region's economy -With the boom of salicornia cultivation in farms and villages around Lake Urmia, suitable employment has been created for the residents of the region and the migration of young people from rural areas to cities to find jobs and income, which gradually reduces local residents, to prevent The action comes. According to the Natural Resources Organization of East Azerbaijan Province, the cultivation of Halknum shrub is one of the ongoing projects. However, since this cultivation is very expensive and in addition the growth time of the plant is not suitable for farmers, plant cultivation such as Salicornia in the lands around Lake Urmia, due to the shorter time required for growth compared to Halknum and yield The product is suitable for agriculture and is recommended Therefore, the hypothesis of cultivation of this species in saline areas around Lake Urmia can be both ideal for farmers and to prevent soil erosion can play a significant role

Keywords: Urmia lake land, Salicornia plant, fine dust Preface

Protective Effect of N-acetylcysteine on Sperm and Biochemical Parameters against Zinc oxide nanoparticles toxicity in Mice (Research Paper)

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Introduction: Zinc oxide nanoparticles (ZnO NPs) are one of the most widely used nanoparticles in the industry, medicine, pharmacy, cosmetic and nutrition. Due to the widespread use of ZnO NPs in various industries, evaluation of toxic effects of this nanoparticle in biological systems, espacially its effects on male reproductive organs and fertility potential are essential. Studies have shown that antioxidants can reduce the harmful effects of nanoparticles. N-acetylcysteine has gained considerable interest as a reactive oxygen species cleanser have shown, that is the potential for its antioxidant effect. The aim of this study was to investigate the effect of N-acetylcysteine as a potent antioxidant on the adverse effects of ZnO NPs on sperm parameters and biochemical factors.

Methods: In this study, 24 adult male NMRI mice (37±2gr) were randomly divided into four groups (n=6) consist of control group (saline, 1 ml/kg), group treated with Zno NPs (50mg/kg/day), group treated with N-acetylcysteine (150mg/kg/day) and group treated with N-acetylcysteine (150mg/kg/day) + Zno NPs (50mg/kg/day). After 28 days of intraperitoneal treatments, sperm parameters and oxidative stress factors were measured. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey's test.

Results: Injections of ZnO NPs significantly reduced sperm count ($P<0.001$), progressive motility percentage ($P<0.05$), viability ($P<0.001$), total antioxidant capacity ($P<0.001$), the amount of serum testosterone ($P<0.001$) and LH level ($P<0.001$) and increased plasma MDA level ($P<0.001$) compared to the control group. In the group of N-acetylcysteine + ZnO NPs, N-acetylcysteine improved the effect of ZnO NPs on Sperm and Biochemical Parameters compared to the ZnO NPs group ($p<0/01$) and improved to the control group. These parameters did not show any significant differences between the control group and the group that received N-acetylcysteine alone ($P> 0.05$).

Conclusion: According to this study, N-acetylcysteine could prevent the adverse effects of ZnO NPs on sperm parameters and biochemical factors by reducing oxidative stress.

Keywords: ZnO NPs, N-acetylcysteine, sperm, oxidative stress,biochemical parameters, Mice.

Protective effects of cornus mas extract on in vitro fertilization potential in methotrexate treated male mice (Research Paper)

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Introduction: Current study was aimed to evaluating protective effects of cornus mas fruit extract (CMFE) in mice treated with methotrexate (MTX)

Methods: 48 young mature male mice were divided into 6 groups. Control group received only normal saline (0.1 mL per day, intraperitoneally), and the second group was administered MTX (20 mg kg-1 per week, intraperitoneally). The third, fourth and fifth groups received MTX daily oral doses of 250, 500 and 1000 mg kg-1 CMFE as well as MTX. The sixth group was only given CMFE with a dose of 1000 mg kg-1 per day, orally, for 35 days. Then, the animals were anesthetically euthanized and the sperms were separated from epididymis. DNA damage level, the amount of malondialdehyde (MDA) as well as in vitro fertility was evaluated

Results: The number of sperms with damaged DNA and MDA level in MTX-treated group showed a significant increase compared to control group ($p < 0.05$). In groups receiving CMFE along with MTX, DNA damage level and MDA amount suggested a decrease in comparison with MTX group ($p < 0.05$). Also, in vitro fertilization and embryonic development in MTX-treated group was significantly lower than the control group, and the level of embryonic arresting was higher ($p < 0.05$). In groups which received CMFE along with MTX, in vitro fertility and embryonic development was higher than MTX group ($p < 0.05$) and the arrested embryos showed a decrease

Conclusion: This study suggested that cornus mas is able to ameliorate the side effects of MTX

Keywords: Cornus mas In vitro fertilization Methotrexate Mice Sperm quality

Protein applications in cosmetic products (Review)

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1.
2.

Introduction: Proteins have various uses in various industries. One of their uses is in cosmetic products. Proteins can be obtained from plants, animals, and microorganism cells [1]. The history of protein use goes back many years when protein (grain flour, animal blood, milk, and egg whites) was used for cosmetic purposes in all major ancient civilizations [2]. However, the first logical use of proteins in cosmetics dates back to the 1950s [2]. The term cosmeceutical was first coined by Albert Kligman in 1984 to refer to products that are used topically and can make changes to the skin [3]. Availability and economy have been the main criteria for selecting protein sources [2]. However, due to increasing consumer concerns about the safety of animal products, industries have shifted to vegetable proteins [4].

Methods: In this study, the collected information of 7 valid scientific articles with the keywords related to the subject and without time limitation has been used. Articles were collected using the Google Scholar search engine.

Results: There is a strong relationship between cosmetic activity and its physicochemical properties. Studies have shown that the most important characteristics of the cosmetic activity of proteins and their hydrolysis are substantivity with the surface of the hair and skin. The outermost layer of skin and hair is made of more or less compressed keratin. Substantivity is related to the ability to make weak or strong bonds with the stratum corneum or hair cuticle. When using proteins and their hydrolyzates, a layer of polypeptides forms on the surface of the skin and hair. Few studies have confirmed the ability of molecules with a molecular weight of less than 3,000 Da to penetrate deeper into the skin (dermis) and hair (cortex). Experiments have shown that peptides can easily penetrate the cuticle and tend to accumulate in the cortex [5]. Proteins and their hydrolyzates can be used as cell growth stimulation in cosmetic products. Another property of proteins in cosmetic products is the strengthening effect of foam on them. Water-soluble proteins, like other hydrophilic polymers, stabilize the foam. They also have anti-irritant, buffering, and viscosity control properties and soften the skin and hair [5]. In cosmetic products, proteins and their hydrolyzates are mainly used for moisturizing agents. High molecular weight polypeptides are used as moisturizing film formers, and low molecular weight peptides are used for products that require high substantivity, such as regenerative hair products [5]. Exogenous proteins can bind to detergents to interact with skin keratin to form a colloidal layer to prevent the detergent from penetrating and attacking the skin [6]. Tomita et al. Showed that hydrolyzed protein with a molecular weight of less than 1000 Da can stimulate the proliferation of human skin cells and is effective for hair and skin conditioning [7]. Less molecular-weight hydrolyzed proteins may be able to protect the skin less than native proteins. The purpose of adding proteins to cosmetic products is mainly as a moisturizing, adsorbing, film forming, or protective

properties. The film-forming properties of cosmetic products (emulsion and foam) are the most important properties for conditioning and cleansing [6].

Conclusion: The cosmetics industry is one of the growing industries in the world. Natural proteins extracted from animal and vegetable sources, with the appropriate characteristics mentioned above, can be used as functional components in the formulation of cosmetic products.

Keywords: cosmetics industry, protein, natural resource, skin and hair care

Psychedelics, Depression be gone (Review)

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Introduction: In recent years there has been an uprising in various methods of treatment for clinical depression and anxiety, in particular the use of ancient and perhaps shunned substances such as psychedelics including Psilocybin, LSD and DMT have come into play and many studies and clinical trials have proved them beneficiary for patients, especially those who were deemed otherwise helpless and were unresponsive to mainstream treatments. This is an overall review of the clinical trials and research studies done so far and a plea for some open mindedness and nuance from colleagues and officials.

Methods: All the various types of clinical trials and research methods have been utilized in the studies and trials that I have cited in my article.

Results: Almost all results have conclusively been that utilizing psychedelics for the treatment of clinical depression and anxiety in patients have had either extraordinary benefits or benefited the patients enough to warrants serious consideration of making the treatment mainstream and accessible to all.

Conclusion: There must be new regulations and funds set in place for further proving the results and making the treatments available to patients all around the world.

Keywords: Treatments, Research, Psychedelics, Medical professionals.

Psycho social experiences of oocyte donors during the donation process : a qualitative study (Research Paper)

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Introduction: In recent decades, one of the most prevalent methods for the couples who, for various reasons, have little chance of conceiving with autologous oocytes is the use of oocyte donation in assisted reproductive technology. This techniques that can undermine the mental health of the women donor. Therefore, the present study aimed to explain the experiences of Iranian oocyte donors during the donation process.

Methods: Data were collected from a hospital-based IVF clinic located in Isfahan city in Iran on 30 oocyte donors. Semi-structured interviews were audio-taped and transcribed verbatim using inductive content analysis method. Purposeful sampling was performed with the strategy of selecting the maximum diversity samples.

Results: Analyzing the data, the three main categories of decision-making challenge, the consequences of participation in assisted reproductive treatment, and the contrast between the self-image and social-image of the donor were inferred.

Conclusion: The findings of the study showed that while donor women consider the spiritual side of their donation, they imagine others' negative view towards it. Therefore, in order to create a positive experience of the donation process, the design of an intervention programs for the promotion of physical and psychological health of the donors seems to be essential.

Keywords: Oocyte donor; Qualitative study; Assisted reproduction technique

Psychological Interventions in Children with Sexual Abuse History: A Comprehensive Literature Review (Review)

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Introduction: Sexual abuse is one of the most common abuses among children while they are the most sensitive group in a society. The Prevalence of child sexual abuse was mentioned about 34% and 8-15% in the world and Iran. Various interventions have been done in children with sexual abuse history; therefore this study aims to review on the effect of psychological interventions in children with sexual abuse history.

Methods: This is a review article. The author applied Google Scholar, especially Persian databases such as SID and Magiran and English databases such as Scopus, PubMed, Web of Science and Science Direct by keywords as child neglect, child sexual abuse, sexual abuse and psychological interventions in MeSH, in addition to the searched articles referred to years 2002 - 2017. From the 2,851 articles that were obtained using the search strategies, 2397 studies were retained after the duplicates and 311 studies were removed after the irrelevant. After the abstracts of the articles were reviewed, 102 studies were excluded, while 10 studies were excluded after the full text was examined. Finally, 31 studies were selected to write this review study.

Results: The psychological interventions in children with sexual abuse history included cognitive behavioral therapy, mindfulness, acceptance and commitment therapy, supportive group therapy, coping skills training, problem solving and stress management. Reviewing the studies indicated that cognitive behavioral therapy and mindfulness, among the mentioned psychological interventions, were the most conducted interventions in children with sexual abuse history. In addition too, the papers indicated that all conducted psychological interventions improved and decreased psychological symptoms, especially stress, anxiety, depression and posttraumatic stress disorder, in children with sexual abuse history.

Conclusion: According to the findings of psychological interventions effect on improving and decreasing psychological symptoms, it is suggested use the psychological interventions conducting by health service providers in order to sexual abuse and improve the quality of life among children.

Keywords: sexual abuse, child sexual abuse, child neglect, psychological interventions

psychosocial attitudes and experiences of oocyte donors: a systematic review (Review)

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Introduction: The number of oocyte donation treatments to overcome infertility has drastically increased since its introduction 30 years ago. Oocyte-donation is generally safe but may exacerbate psychiatric symptoms in some women. This study was conducted to assess oocyte donors' attitudes, motivations and experiences to obtain information on base rates of various experiences associated with oocyte donation.

Methods: A bibliographic search of English and Persian language publications of four databases "web of sciences, Medline, Scopus and SID was undertaken with no time restriction set for publications.

Results: There were 74 studies which met the inclusion criteria and were included in the systematic review. Studies showed that a significant proportion of oocyte donors were prepared to donate their oocytes as identifiable donors. The research syntheses revealed there were distinct differences between motives for donation, and issues relating to disclosure. Further, most studies on the attitudes and feeling of patients involved from all sides of the donation process were extremely positive.

Conclusion: In general terms this review explored, the attitudes and feeling of patients involved from all sides of the donation process were extremely positive and despite the hazards and discomfort of the oocyte donation procedure, the majority of donors have reported positive experiences of oocyte donation.

Keywords: oocyte donation, gamete donation, systematic review

Radiolabeling of Anti-HER2 scFv with 99m-Tc tricarbonyl through His-tag (Research Paper)

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Introduction: Breast cancer is the most common cancer and the second cause of cancer death in women, worldwide. Recently, invasive biopsy method is used for detection of benign from malignant tissues. Correlation between breast cancer malignancy and human epidermal growth factor 2 (HER2) overexpression has led to the application of monoclonal antibodies targeting HER2 receptors in treatment and diagnosis of HER2-overexpressing breast cancer. Single chain variable fragment (scFv) contains variable regions of heavy and light chains of an antibody and is the smallest functional region of an antibody for antigen binding. The penetrability of scFvs into tumors is improved while its specific affinity is retained and its immunogenicity is lowed as compared to full length antibody. scFv against HER2 can be conjugated to radioisotopes for staging and diagnosis of HER2-positive breast cancers and their metastasis. 99mTc is used in over 98% of radiopharmaceuticals. Its optimal nuclear properties including short half-life (6 h), decomposition through isomeric transition (IT), gamma photon emission of 140 keV, availability via 99Mo/99mTc generator and known chemical properties make 99mTc a suitable radionuclide for diagnostic applications in nuclear medicine. Technetium-99m forms very stable complexes in its inert stable +1 oxidation state in the form of aqueous 99m-Tc-tricarbonyl with His-tag which is used as purification tag for immobilized metal affinity chromatography (IMAC). 99mTc(I) tricarbonyl provides high labeling yield and the least damage to biological activity of scFv. The aim of this study is to label anti-HER2 scFv with 99m-Tc-tricarbonyl and evaluate the effect of radiolabeling on biological activity of anti-HER2 scFv.

Methods: Anti-HER2 scFv gene was expressed in Escherichia coli BL21 (DE3) host. Anti-HER2 scFv protein was then purified by IMAC under native condition. Anti-HER2 scFv was directly labeled by techneyium-99m tricarbonyl. Radiochemical purity (RCP¬%) was determined using thin layer chromatography (TLC) and high-pressure liquid chromatography (HPLC). Biologic activity of anti-HER2 scFv and 99m-Tc-anti-HER2 scFv was evaluated by HER2-based ELISA.

Results: Highly pure anti-HER2 scFv with approximately 28 kDa molecular weight was obtained by IMAC using Ni-NTA resin under native condition. RCP% of

radiolabeled anti-HER2 scFv (99m-Tc-anti-HER2 scFv) was approximately around 98%. HER2-based ELISA demonstrated no significant difference between the biologic activity of anti-HER2 scFv and 99m-Tc-anti-HER2 scFv.

Conclusion: Anti-HER2 scFv was directly radiolabeled by 99m-Tc- tricarbonyl. Based on the results, 99m-Tc-anti-HER2 scFv is a proper candidate for specific targeting of HER2 receptor and can be used for diagnosis of breast cancer type, detecting metastasis and evaluation of treatment efficacy in HER2 overexpressing-breast cancer.

Keywords: Breast cancer, HER2, scFv, Radiolabeling, Technetium-99m tricarbonyl

Radiomics in hepatocellular carcinoma (Review)

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Introduction: Hepatocellular carcinoma (HCC) is the most common liver cancer that mostly occurs in patients with chronic liver disease such as cirrhosis or severe fibrosis. Its major causes are chronic liver disease due to chronic hepatitis B and C virus infection or metabolic liver disease. HCC often becomes symptomatic only at an advanced stage when curative treatments are no longer possible. Therefore, the prognosis of HCC remains unsatisfactory. Radiomics is an emerging field which extracts quantitative radiology data from medical images and explores their correlation with clinical outcomes in a non-invasive manner. It aims to quantify the morphological appearance of the tumor, i.e., its imaging phenotype, using mathematically defined quantitative features. The aim of this study was to investigate whether radiomics is a useful and prognostic method for clinical management of hepatocellular carcinoma

Methods: In this study, we reviewed and searched for the keywords "hepatocellular carcinoma", "HCC", "medical imaging" and "radiomics" in the scientific databases of Science Direct, PubMed and Google Scholar. About 10 fully relevant articles were found and reviewed.

Results: Several medical imaging modalities such as computed tomography, magnetic resonance imaging, and positron emission tomography were used for radiomics features extraction. The results of all studies showed that the heterogeneity, grade, and malignancy of HCC lesions can be assessed with high accuracy by using radiomics analysis of medical images. Also, the combination of mathematical radiomics features with clinical genomic features can lead to better results.

Conclusion: Radiomics is a completely non-invasive method and can be a complementing or replacing approach for tumor biopsies, as well as for developing novel prognostic biomarkers in HCC patients in the near future.

Keywords: radiomics, hepatocellular carcinoma, medical imaging

Radioprotective Effect of Pioglitazone against Genotoxicity Induced by Ionizing Radiation in Healthy Human Lymphocytes (Research Paper)

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Introduction: Objective: Pioglitazone (PG) is used to control high blood sugar in patients with type 2 diabetes mellitus. PG acts as a peroxisome proliferator - activated receptor γ agonist. In addition to the insulin-sensitizing effect, PG possesses anti-inflammatory effect. In this study, the protective effect of PG was evaluated against DNA damage induced by ionizing radiation in healthy human lymphocytes.

Methods: The microtubes containing human whole blood were treated with PG at various concentrations (1 -50 µM) for three hours. Then, the blood samples were irradiated with X-ray. Lymphocytes were cultured for determining the frequency of micronuclei as a genotoxicity biomarker in binucleated lymphocytes.

Results: The mean percentage of micronuclei was significantly increased in human lymphocytes when exposed to IR, while it was decreased in lymphocytes pre-treated with PG. The maximum reduction in the frequency of micronuclei in irradiated lymphocytes was observed at 5 µM of PG treatment (48% decrease).

Conclusion: The anti-inflammatory property suggested the mechanism action of PG for protecting human lymphocytes against genotoxicity induced by ionizing radiation.

Keywords: Anti-inflammatory, micronucleus test, pioglitazone, radiation biology, radioprotective.

Rapid hemostasis by nanofibrs of polyhydroxyethyl methacrylate / polyglycerol sebacic acid: Fabrication, characterization, cytotoxicity and effectiveness on bleeding animal model (Research Paper)

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Introduction: Uncontrollable hemorrhage is a primary reason for death in war, car accidents, and surgical procedures. Dehydration of blood causes half of the death in war. It is reported that more than 30% of deaths occur in 5-10 minutes as bleeding originates of hemorrhagic shock in pre-hospital emergency services. The fast bleeding control method does not only reduce death but also help to achieve optimal recovery. Bleeding control includes mechanical barriers or chemical inducing hemostatic pathways to help the natural blood coagulation process. Polyglycerol sebacic acis(PGS) is a biodegradable polymer, which is also widely used in tissue engineering and wound heling. This polymer is recommended for soft tissue engineering because it has elastomeric properties, biocompatibility, linear degradation rate, and nontoxic products. Polyhydroxyethyl methacrylate (PHEMA) is another biodegradable and biocompatible polymer used in tissue engineering. PHEMA has been used to prepare sponges, which can adhere to blood proteins and is also used to prepare spherical, porous particles containing ethamsylate and aminocaproic acid, the hemostatic drugs for embolization. Tranexamic acid (TA) is generally administered as capsule from oral route to control menorrhagia. It has a bitter taste and gastrointestinal side effects. Intravenous route is used in surgeries but it has thromboembolism risk and gets slow to therapeutic level. On the other hand TA has shown positive wound healing effect. Due to the low plasma level in topical use, direct topical use of TA in hemorrhage can reduce bleeding volume and bleeding time without systemic side effects. The purpose of the present study was designing nanofibers of PGS/PHEMA loaded with TA for homeostasis to reduce the severity and bleeding time.

Methods: Glycerol and sebacic acid were mixed with a molar stoichiometric ratio of 1:1 and stirred at 120 ˚C in a nitrogen atmosphere for 24h and pressure less than 50 mTor. Porous nanofibers of polyglycerol sebacate (PGS), polyhydroxyethyl methacrylate (PHEMA) and tranexamic acid (TA) were prepared by electrospinning method. The nanofibers were optimized for their morphology, diameter size, porosity, TA loading, release profile, hydrophilicity, water absorption and

mechanical behavior. Their cytotoxicity was studied by MTT assay on L929 cells. The hemostasis control on tail cut model in rats was investigated.

Results: The best formulation contained 35% of the total polymers, 20% of PGS and 10% of TA to total polymers. These nanofibers had 64% porosity, 8.59% water sorption and 1.47% weight loss after 28 days with no cytotoxicity on L929 cells. TA loaded nanofibers showed significantly less bleeding volume than other groups, but no significant difference in bleeding time was seen with the blank nanofibers.

Conclusion: The nanofibers of PGS/PHEMA were electrospun and loaded with TA. The processing parameters were optimized to obtain nanofibers with a smooth, bead-less morphology and least diameter. The results demonstrated that the voltage and speed of injection of the solution significantly changed the nanofibers diameter. Increasing the total polymer content of the nanofibers increased thickness of nanofibers. PGS content and TA content of the nanofibers caused improvement of their mechanical behaviors and increasing the PHEMA content of the nanofibers caused more porous structure. By increasing the PGS content the mean pore area increased. The presence of PHEMA provided good hydrophilicity for absorbing the blood and slow biodegradability. The composite nanofibers were non-toxic on mouse fibroblast cells. Rapid drug release, which was completed within a few minutes provided rapid effectiveness of the nanofibers and decreased the bleeding time compared to the control groups. From the obtained results, it may be concluded that the designed dressing of TA may provide a prominent way for hemostasis compared to the conventional treatments of bleeding control, which reduces the risk of hemorrhagic shock by decreasing the volume and time of bleeding and induces faster recuperation of the injuries. The designed nanofibrous dressing may be useful in buccal, mucosal or battlefield and surgeries.

Keywords: hemostats, tranexamic acid, nanofiber, Polyglycerol sebacate , polyhydroxyethyl methacrylate ,

Reasons for Stopping Exclusive Breastfeeding Between Three and Six Months: A systematic review (Review)

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Introduction: Failure to stop exclusive breastfeeding causes the baby to grow fully. It prevents infectious diseases and reduces mortality. This stop has recently increased. The aim of this systematic review is to investigate the reasons for stopping exclusive breastfeeding between three and six months among mothers.

Methods: Search was done by keywords in the databases: Pubmed, Google scholar, Science Direct, in the period of 2000-2020. At the pubmed, 10 articles were received. By studying the title of the articles, 5 articles were selected. By studying the abstract of the articles, 2 articles were selected. At the Google Scholar,25 articles were obtained,2 articles were included. At Science Direct12 articles were in English2 review articles were identified and all removed .Finally we review 6 articles in this study.

Results: Six experimental studies were reviewed. A study of 30 women in New Zealand found that some mothers returned to work due to the effects of short-term maternity leave on breastfeeding. Mothers strive to balance breastfeeding, personal needs, and social activities and psychological factors in the family. In a study of 500 women, the most common reasons for stopping breastfeeding were discomfort and fatigue from breastfeeding, as well as concerns about milk supply and returning to work or school. It was stated in a general study lack of support; physical or emotional health of the mother; maternal choice; and insufficient milk supply. Some studies show that nipples pain are a common problem in breastfeeding, as well as health conditions such as postpartum depression, fatigue and acute health problems. A South African study found that among babies with HIV, breastfeeding stops in the first six months of life and weight loss occurs.

Conclusion: Most articles have reported that women are under social pressure and do not receive enough support. Studies show mothers are influenced by a variety of factors when making decisions for stopping exclusive breastfeeding, including social constructionism and economic norms and the experiences of others. The use of results will help inform future research aimed at identifying interventions to reduce early breastfeeding

Keywords: Exclusive breastfeeding ،Breastfeeding support ،Social constructionism

Reducing greenhouse gases by modifying the genetic structure of cyanobacteria (Research Paper)

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Introduction: In a study conducted at KTH University in Sweden, they were able to produce refined cyanobacteria, carbon dioxide and sunlight, renewable butter, called butanol. In this paper, along with the production of co2 production plants, this laboratory is designed to grow cyanobacteria by modifying the genetic structure and producing butanol, It uses butanol for fuel for the power plant. One of the challenges facing humans is the increase in the heat of the earth due to the increase in greenhouse gases, especially CO2. I was studying the transfer of life to other planets using bacteria, a study conducted at KTH University in Sweden. The study, led by Paul Hedson, modified the genetic structure of cyanobacteria to alter the natural metabolism of these bacteria to produce butanol. By correcting the relevant genes in the cyanobacterial genome, they could deceive cyanobacteria. They produce butanol instead of their natural process. I have come to the conclusion that it will be built alongside with the laboratories producing CO2, In this laboratory , cyanobacteria are being cultivated with genetically modified structure using CO2 and sunlight and butanol production, and use butanol to generate electricity

Methods: In this article, it is explained that next to the factories that produce carbon dioxide, tanks are placed in which the carbon dioxide produced by these factories is placed. Next to these tanks, we place glass greenhouses containing large erlens containing genetically modified bacteria that produce butanel. It then transports the carbon dioxide in these tanks to large erlens, as well as sunlight, which is a growth factor for these bacteria and thus produces butanel. Then next to this glass greenhouse containing the large Erlenmeyer is a power plant that works with butanel, just like the power plants in Brazil that run on ethanol.

Results: As explained in the article, it can be concluded that using genetic modification of bacteria to reduce the amount of carbon dioxide on Earth and generate electricity from butane, which is a renewable fuel.In fact, with this method, we can significantly reduce greenhouse gases. Increasing greenhouse gases is one of the problems of climate change, which in this way not only reduces it but also generates electricity from the fuel produced.

Conclusion: In fact, this article explains that by modifying the genetic structure of cyanobacteria, we can link the natural metabolism of cyanobacteria to the production of butanel. In fact, by modifying the relevant genes in the genome of cyanobacteria, we can trick cyanobacteria into producing butanel instead of its natural process.The positive point of butanol is that its raw materials are found in abundance and are renewable, and also butanol can be obtained 20 times more than sugarcane or corn stalks.

Keywords: Butanol - CO2

Relationship between Cardiovascular Diseases and Vitamin D Deficiency (Review)

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Introduction: Cardiovascular risk factors, such as arterial hypertension, obesity, dyslipidemia or diabetes mellitus, as well as cardiovascular diseases, including myocardial infarction, coronary artery disease or stroke, are the most prevalent diseases and account for major causes of death worldwide. Vitamin D (25-OH-cholecalciferol) deficiency, as well as cardiovascular diseases and related risk factors are highly prevalent worldwide. The scope of this review is to provide a brief overview on basic vitamin D metabolism and vitamin D deficiency. This study reviews the most recent studies evaluating the relationship between vitamin D and the presence of cardiovascular risk factors. This underlines the importance of clarifying the role of vitamin D in the context of cardiovascular diseases.

Methods: In the current study, key words including vitamin D (25-OH-cholecalciferol), cardiovascular disease and cardiovascular risk factors were reviewed from the list of Mesh and other credible websites, including PubMed, Science Direct and Google Scholar, over the past two decades and the desired data was organized.

Results: Vitamin D exerts biological effects on cardiac myocytes, stimulating calcium-ATPase activity and calcium uptake in cardiac myocytes. Lack of vitamin D could cause diastolic dysfunction. vitamin D deficiency stimulates systemic and vascular inflammation, enabling atherogenesis. on the other hand, as already mentioned, hypertension is also associated with lack of vitamin D, due to activation of the renin-angiotensin-aldosterone system, enabling endothelial dysfunction, the first step in plaque formation. Vascular smooth muscle cells and endothelial cells express receptors for vitamin D, enabling conversion of calcidiol to calcitriol and vitamin D is involved in regulation of growth and proliferation of smooth muscle cells and cardiomyocytes. Vitamin D inhibits the proliferation of vascular smooth muscle cells by acute influx of calcium into the cell and increases calcification of smooth muscle cells. Murine models, lacking vitamin D receptor, exhibit increased ventricular mass, higher atrial natriuretic peptides and impaired homeostasis of metalloproteinases and fibroblasts, leading to ventricular dilatation and impaired electromechanical coupling.

Conclusion: Maintaining an optimal vitamin D serum level seems important not only for calcium homeostasis but also for cardiovascular risk, blood pressure control, prevalence of stroke, metabolic syndrome, and peripheral artery disease. Observational data support the relationship between vitamin D status and

cardiovascular diseases and vitamin D deficiency can be considered a cardiovascular risk marker.

Keywords: vitamin D (25-OH-cholecalciferol), cardiovascular disease, cardiovascular risk factors.

Relationship between knowledge about HIV/AIDS and preventive action against in medical and dentistry students (Research Paper)

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Introduction: Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) is a spectrum of conditions caused by infection with the human immunodeficiency virus (HIV). Following initial infection a person may not notice any symptoms, or may experience a brief period of influenza-like illness. Typically, this is followed by a prolonged period with no symptoms. There were an estimated 38.0 million people living with HIV at the end of 2019. Due to gaps in HIV services, 690 000 people died from HIV-related causes in 2019 and 1.7 million people were newly infected. W.H.O. defines key populations as people in populations who are at increased HIV risk in all countries and regions. Key populations include: men who have sex with men; people who inject drugs; people in prisons and other closed settings; sex workers and their clients; and transgender people. Increased HIV vulnerability is often associated with legal and social factors, which increases exposure to risk situations and creates barriers to accessing effective, quality and affordable HIV prevention, testing and treatment services. There is no cure for HIV infection. However, effective antiretroviral drugs (ARVs) can control the virus and help prevent onward transmission to other people. Since scientists haven't found an effective treatment of HIV/AIDS and outbreak of it increasingly in world prove necessity of knowing the prevention and transferable ways of HIV/AIDS especially for persons who are in contact with blood and blood products such as medical and dentistry students.

Methods: 150 questionnaires were send to medical and dentistry students who were in the practical work phase and were in contact with the patient and patients' blood or secretions to be completed by them. Out of 150 questionnaires, 114 were completed and returned. Questionnaire A had 20 questions that assessed students' knowledge about HIV/AIDS: the first 10 questions were in the field of disease recognition, the next 5 questions were related to the ways of transmission and the last 5 questions were about disease prevention. Questionnaire B had 15 questions related to students' preventive performance at work and in contact with patients or patients' fluids. Each question had 3 answers, with the option "always" has +2 points, "sometimes" +1, and "never" has zero point.

Results: In the questionnaire A out of 114 answers, the maximum correct answers was 18 out of 20, and minimum 8 out of 20 with a mean of 12.1 and a standard deviation of 2.63. In the questionnaire B out of 114 answers, the maximum correct

answer was 27 out of 30, and minimum 8 out of 30 with a mean of 19.6 and a standard deviation of 4.7.

Conclusion: 1- Preventive act of students will be increase with expanding of knowledge and there is significant relationship between these two agents. 2- 57.9 % of students has little or low knowledge about HIV/AIDS and 44.7 % has slight or very little preventive act. 3- There was not significant relationship between knowledge of students and sex but between preventive act rate and sex was significant. 4- Significant relationship was noted between rate of knowledge and background of dangerous contact but not between preventive act and background of dangerous contact.

Keywords: knowledge, preventive action, HIV/AIDS

Relationship Between Premature Menopause-related Genetic Polymorphisms and Level of Serum Micronutrients (Research Paper)

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Introduction: Permanent menstrual cessation in women under 40 years old, is called Premature Menopause (PM). The last data indicated that the prevalence of this condition is about 65 percent higher in Iranian women than meta-analyzed estimates of all females around the world that might be related to earlier age at menarche in Iranian girls and lower age of developing ovarian cancer in Iranian females that requires treatments that could lead to PM. Genome-Wide Association Studies (GWAS) and some other epidemiological investigations found that some specific polymorphisms are highly significantly prevalent in PM cases than healthy controls. Moreover, it has been found that micronutrients including vitamin D, calcium, zinc, and copper are associated with PM and could be related to women reproductive tract. In the present study, we have investigated the association between some known PM-related Single Nucleotide Polymorphisms (SNPs) and important micronutrients serum level.

Methods: 117 PM cases along with 183 controls were selected from Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) cohort study. PM diagnosis was established by the following criteria: 1) Menstruation cessation for 12 consecutive months, 2) Age under 40, or 3) Follicle-Stimulating Hormone (FSH) elevation (>40 IU/L) for 3 times (repeated at four-week intervals). In order to assess the SNPs of PM cases and comparing them to healthy controls, we used Allele-Specific Oligonucleotide Polymerase Chain Reaction (ASO-PCR) and Tetra Amplification Refractory Mutation System PCR (ARMS-PCR) methods. Serum level of vitamin D (25-hydroxy vitamin D), copper, zinc, calcium, phosphate, and magnesium were measured using standard methods. Finally, the data were analyzed by SPSS, version 24. By Kolmogorov-Smirnov (KSV) test, all variables were checked for normal distribution. Association of SNPs' genotypes and serum level of micronutrients was examined in PM cases and healthy controls, separately by Man-Whitney analysis. Multivariable logistic regression was performed to determine the relationship between two major genotypes of each SNP and micronutrients serum levels' categories, in an adjusted model for age and Body Mass Index (BMI) confounding variables.

Results: Our study found that following SNPs' genotypes are significantly different between cases and controls: rs4806660 (TMEM), rs451417 (MCM8), rs16991615 (MCM8), rs7246479 (BRSK1), rs244715 (ZNF346), and rs10183486 (TLK1). Serum copper, phosphate, and calcium level were considerably different among the

genotypes of rs244715, rs451417, and rs4806660 SNPs, respectively in the PM subjects; While in controls, we found that just copper is different meaningfully in level between rs4806660, rs7246479, rs1046089, and rs2303369 SNPs' genotypes. After adjusting the effect size of other genotypes, age, and BMI, we recognized that in PM cases regarding rs4806660 SNP, decreased serum copper concentration was found 78% lower in TC cases than TT ones. Moreover, in assessing rs244715, serum level of copper was significantly elevated in GG genotype PM cases than cases with AA genotype. These significant differences were not found for controls.

Conclusion: It seems that according to previous investigations, SNPs related to PM are associated with hormonal changes, especially sex hormones, and alterations in metabolic factors. Moreover, it was indicated that sex hormone therapy could cause minor changes in copper level; Indeed, primary ovarian insufficiency, which is a known condition that could lead to PM, is associated with serum level of copper. Thus, it might be concluded that PM-related SNPs could cause changes to sex hormones and these hormones might affect the concentration of copper in these cases. In this study, rs4806660 and rs244715 genotypes were found to be related to abnormalities in PM cases' serum copper level.

Keywords: Premature menopause; Micronutrients; Copper; Medical genetics; Polymorphisms

Retinoic Acid and Fibroblast Growth Factor-2 Play a Key Role on Modulation of Sex Hormones and Apoptosis in a Mouse Model of Polycystic Ovary Syndrome Induced by Estradiol Valerate (Research Paper)

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Introduction: The main goal of the present study is to investigate the effects of retinoic acid and fibroblast growth factor-2 on serum levels of FSH and LH, histology, and apoptosis in the mouse model of Polycystic Ovary Syndrome (PCOS).

Methods: 80 female NMRI mice have been randomly divided into eight groups. Group 1 received normal saline as a control, and Group 2 received estradiol valerate (EV) at 4 mg/100 g of body weight. Moreover, Groups 3-4 were administered with RA (a dose of 0.05µg/µl) and FGF2 (a dose of 0.01µg/kg), respectively. Groups 5 and 6 respectively received the EV plus the RA (0.05µg/µl) and FGF2 (0.01µg/kg). Group 7 received the RA and FGF2 at doses corresponding to healthy mice, and Group 8 received the EV plus the RA+FGF2 (similar to previous doses). RA and FGF2 were injected three times per week for four weeks. Finally, histological and immunohistological parameters of the ovary were evaluated.

Results: The study revealed that both single and combined injection of fibroblast growth factor-2 (FGF2) and retinoic acid (RA) in groups 5, 6, and 8 significantly reduced follicular diameters compared to group 2. Measurements confirmed that simultaneous injection of RA and FGF2 into polycystic mice significantly increased antral follicles, corpus luteum (CL), epithelial thickness, and oocyte diameter as well as decreased cystic follicles. Positive TUNEL cells that were considerably increased in the antral follicle of group 2 significantly decreased in the RA and FGF2 recipient groups, either alone or in combination. Besides, the injection of FGF2 increased preantral follicles and CL.

Conclusion: The findings of the present investigation reveal that injection of RA and FGF2 has both protective and ameliorative effects that can promise new therapies for women with PCOS.

Keywords: Retinoic acid, Fibroblast growth factor-2, PCOS, Sexual hormones, Apoptosis, Mouse.

Review and comparison of treatment and effectiveness of some methods of treating brain cancer (Review)

Razieh Eini,[1,*]

1.

Introduction: Introduction: Meningioma and glioma are the most common and malignant cancers of the brain, respectively. Proton therapy in meningioma and glioma shows significant thematic control and it has low side effects and thus has an example on the patient's quality of life. Clinical data are limited in carbon therapies (CIRT) however, the available information confirms the reduction of toxicity and side effects of this method and the high degree of local control of this method. Proton therapy and carbon therapy are used continuously in the treatment of glioma, and in this disease, it is more possible to use high-dose radiation. However, many studies are needed for the therapeutic effects of both methods and the effect on cognitive approaches and neural functions. Hyperbaric oxygen therapy (HBO) is also used as an adjunct therapy for some brain cancers and is done as a way to overcome tissue oxygen depletion. Hypoxia is one of the causes of ineffectiveness of clinical treatments. HBO can be effective in treating malignant gliomas, and combining this method with radiotherapy can be more effective than radiotherapy alone, as well as reducing the side effects of cytotoxic chemotherapy drugs.

Methods: Method: In this study articles related to brain cancer in recent years was searched from the pubmed database. The clinical results of various studies and treatments for two common types of brain cancer, including meningioma and glioma, were evaluated.

Results: Result: According to the general results of research, some adjunctive therapies, including radiotherapy, may cause complications such as thromboembolism due to the sensitivity of the cerebral arteries. The results of chemotherapy research studies show that some chemotherapy drugs may cause micrometastasis in the brain. and in general, chemotherapy drugs in brain cancer create a brain environment for the growth of brain tumors.

Conclusion: Conclution: In general, traditional methods of treating cancer, including radiotherapy and chemotherapy, can not be successful in treating brain cancer. Treatment of various types of brain cancers requires further research and new therapies. Some results of nanoscience treatment have shown significant effectiveness. Nanodrugs and nanoparticles have shown significant results in treatment due to the sensitivity of Cerebral vessels and blood brain barrier. And these treatments seem to have acceptable results in combination with other methods such as proton therapy and carbon therapy and other methods.

Keywords: meningioma, glioma, hypertensive oxygen therapy, adjunctive therapie

Review of 2D and 3D cell cultures (Review)

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Introduction: Cell culture is an important in vitro tool to use in different studies such as cell behaviors, drug screening and gene expression.2D cell cultures are used because they are an economical and convenient method. However, they cannot accurately reflect tumor microenvironment. To overcome these limitations, three-dimensional spheroid culture models have developed. In this review article /we compare 2D and 3D culture methods.

Methods: A targeted search has been performed on 3 websites: PubMed, science direct and goggle scholar. Article information has collected from English articles.

Results: In2D culture, cells grow as monolayer in a rigid plate and cells adhere to surface of plate only one side. Thus, there is defect of interconnections between cells and extra cellular matrix (ECM) surrounding them. Gradients of Oxygen, nutrients and waste do not exist and all cells have access oxygen and nutrients. These changes affect the phenotype and behavior of cells. Thus, they cannot simulate the function of living tissues.in 3D cultures ,E-cadherin, actin, microtubules, and FAK are important elements in formation of spheroids. Spheroids due to oxygen, nutrient and waste gradients are divided 3 zones: Necrotic zone, Quiescent viable cell zone and proliferating zone. Proliferating zone is outer layer and has more access to oxygen and nutrients while inside layer has less access to nutrients and oxygen. This structure mimics the physical features of a solid tumor mass .The structure of spheroids has an effect on drug resistance because cells in medium zone have decreased access to drug .Also Because of oxygen gradient in spheroids , inadequate diffusion of oxygen produces hypoxia.in hypoxia up-regulation of VEGF is observed and it can lead to drug resistance. Another reason of drug resistance is up regulation of Cluster of differentiation 44(CD44) in spheroids .Spheroids interact with ECM. Hyaluronan is a main ligand for CD44 and actives It. CD44 regulates some signaling pathways such as PI3/AKT and Ras-MAPK pathways. It has been proven that knocking-out of CD44 by the CRISPR-Cas9 system can inhibit tumor progression, metastasis and ameliorate drug resistance.

Conclusion: There are Differences in morphology, gene expression ,hypoxia and drug resistance in 2D and 3D cultures and resemblance between 3D cultures and living tissues .failures of 2D culture models in drug screening in pre-clinical in vivo tests or clinical trials indicate that It is better to replace two-dimensional culture models with three-dimensional culture models.

Keywords: 2D cultures , 3D cultures,living tissues

Review of prevalence and management of allergenic pollen in Iran (Review)

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Introduction: The importance of pollen grains in developing respiratory allergy has been well documented all over the world. Pollen grains are the most common and the strongest allergy carriers in most countries worldwide, with a high Prevalence rate among allergic patients. While clinical diagnosis of most allergy can be accurately made, specific geographical implicated allergens and predictions of immunotherapy treatment response elude the currently available diagnostic and therapeutic tools for the care of allergy patients across different regions of the world. Therefore, there is a need for the discovery of geographical allergens for accurate disease diagnosis, prognosis and predicting treatment response.

Methods: The aim of this study is to introduce the most allergenic pollen grains in Iran based on published papers in the area and provide a basis for prevention strategies and immunotherapeutic treatments.

Results: . According to available data, allergies to pollen grains comprise up to 86.7% of the allergic patients in various cities of Iran depending on phytogeography and environmental conditions. Three major sources of pollen allergens in different parts of Iran are 1) anemophilous taxa of Asteraceae and Amaranthaceae particularly Artemisia, Kali tragus, Chenopodium album, Bassia scoparia, Amaranthus spp., of which Pollen of Kali tragus induces the highest amounts of allergic rhinitis in Iranian patients, 2) the widespread non-cereal grasses specially Phleum pratense and Lolium perenne and 3) the anemophilous trees such as gymnosperms, Phoenix dactylifera, Prosopis juliflora, Fraxinus excelsior, Olea europaea and Platanus orientalis.

Conclusion: Considering the biological and ecological characteristics of these allergy-inducing plants we conclude that our knowledge of the distribution of these taxa is of little help in identifying the allergen source since most of these plants are ruderal, weeds or ornamental and park trees. In contrast, for the reason that these plant-groups bloom in considerably separate periods, flowering time plays a key role in recognizing the allergen sources, hence taking appropriate preventive policies, providing proper management and applying more accurate immunotherapeutic treatments in allergic patients.

Keywords: Pollen allergy, allergens, anemophilous plants, immunotherapy

Risk Factors of Postoperative Cognitive Dysfunction (POCD) after Oncological Surgery-a systematic review (Review)

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Introduction: Introduction: Postoperative cognitive dysfunction (POCD) is a common morbidity usually after large and medium- sized surgery under general anesthesia and in elderly patients (in fact, it can occur in any ages). It affects many cognitive domains such as memory, information, concentration and attention. It impairs postoperative recovery, increase medical cost for patients, affect the quality of life of patients and also increase mortality. In most oncological cancers, long anesthesia duration, radical resections that cause serious traumas and also inflammatory responses that happens, increase this risk of POCD with high probability. The specific physiopathology and also really effective treatment of POCD are still unclear, so many studies should be done. Aim: In this review, we want to study risk factors of POCD in patients who had cancer and underwent surgery for it.

Methods: Methods and materials: A comprehensive search was done through all types of articles (except reviews and animal and cellular studies) in English in nine databases (PubMed, Google Scholar, Cochrane, Science Direct, Embace, Scopus, ISI, Web of Science and ProQuest) with the keywords of POCD, cancer and surgery and with the 10 years' time filter. For the exclusion criteria study characteristics and report futures were considered. Review methods: All identified articles from different sources were transferred to a database using resource management software to remove duplicates. Two reviewers independently examined the titles and abstracts of the articles using the inclusion and exclusion criteria and checklist by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) . In case of disagreement between the two, the judgment regarding the inclusion of the article in the study was applied with the opinion of a third reviewer.

Results: Results: As inclusion criteria 254 studies were involved that after omitting duplicates 173 studies were remained and by exclusion criteria 33 articles were selected as main studies of this systematic review. In our main studies, 3,884 patients were involved totally, and POCD cases were detected by tests like MMSE and TICS-M. Age, location and structural and biomolecular effects from the tumor, cancer-related anemia, anesthesia regimen, duration of anesthesia, type of anesthesia, perioperative cares and treatments, Inspiratory Muscle Training,

mechanical ventilation, intraoperative blood loss , severity of surgery, the occurrence of complications, and pre-existing cognitive impairments, diabetes history, fasting over 3 days, a Systemic inflammatory response syndrome (SIRS) score of > 3 on the second day, Preoperative hyperhomocysteinemia, vitamin D deficiency, the levels of serum Tumor necrosis factor α(TNF-α), interleukin 6 (IL-6),IL-10, IL-1β, serum amyloid A (SAA), S100 calcium-binding protein β (S-100β), and high mobility group box-1 protein (HMGB-1) , C-reactive protein(CRP), Insulin-like growth factor 1 (IGF-1), Insulin Like Growth Factor Binding Protein 7(IGFBP7), miRNA-155, Phosphoinositide 3-kinases (PI3Ks) and Protein kinase B (AKT) after operation are some factors that affect the occurrence and intensity of POCD.

Conclusion: Conclusions: As the result, demographic factors, history of patient, anesthetic variables, location and structural and biomolecular effects from the neoplasms, perioperative and intraoperative cares and treatments, characteristics of surgery, biochemistry profile of patient's serum are the factors relating to POCD. Science the exact physiopathology of POCD is unknown more cellular studies and comparative studies (between different procedures) are needed.

Keywords: pocd, postoperative cognitive dysfunction, cancer, oncology, surgery

Role of E-cadherin/ β-catenin complex in Chemopreventive and Anti-cancer Efficacy of Silibinin in colorectal cancer (Research Paper)

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Introduction: Colorectal cancer (CRC) is among the top five world's common cancers with high mortality. Silibinin is the most active flavonolignan constituent of Silymarin, the extract of milk thistle seeds. Epithelial-mesenchymal-transition (EMT) and Cancers stem cells (CSCs) are known to contribute to cancer initiation, progression and metastasis. In this study, we investigated the anti-cancer properties and molecular mechanisms of Silibinin on proliferation, apoptosis, the CSCs markers, EMT process and migration in vitro.

Methods: HCT-116 cells were treated with 50 μM of Silibinin for 24 and 48h to investigate its effects on proliferation, migration, EMT, CSCs, apoptosis and involved mechanisms by using MTT and colony formation assay, Acridine orange/propidium iodide double staining, sphere formation assay, RT-qPCR, Western blot and wound healing assay. One-way variance analysis (ANOVA), followed by Tukey–Kramer pairwise comparison, was performed to determine the significance of the difference between groups, using SPSS 25.0 software.

Results: : Silibinin significantly suppressed the proliferation of HCT-116 cells ($p<0.001$), while had no toxic effect on normal cells. Silibinin induced apoptosis by increasing the Bax/Bcl-2 ratio in cancer cells ($p<0.001$). Furthermore, the mRNA expression of cancer stemness markers; cluster of differentiation 133 (CD133), cluster of differentiation 44 (CD44), BMI1, Aldehyde dehydrogenase 1 (ALDH1), and doublecortin-like kinase 1 (DCLK1) was considerably decreased in treated HCT-116 cells with Silibinin ($p<0.001$). Moreover, Silibinin attenuated EMT by decreasing the mRNA expression of neural cadherin (N- cadherin) ($p<0.001$) and vimentin ($p<0.001$) and increasing the mRNA and protein expression of epithelial cadherin (E-cadherin) ($p<0.001$). The mRNA and protein expression of β-catenin was decreased in treated cells with Silibinin as well ($p<0.001$). Silibinin decreased the mRNA expression of MMP-2 ($p<0.001$) and MMP-9 ($p<0.001$) and inhibited cell migration in a time- and dose-dependent manner.

Conclusion: Our study revealed that the anti-cancer properties of Silibinin is mainly due to its ability to induce apoptosis, eliminate CSCs, attenuate EMT related markers and inhibit migration of CRC cells. It seems that Silibinin exhibits these anti-tumor mechanisms through blocking β-catenin molecule, which is a key component of the Wnt signaling pathway, one of the hallmarks of CRC development.

Keywords: Silibinin, Colorectal cancer, Epithelial-mesenchymal-transition, Cancer stem cell, β-catenin

Role of Escherichia coli infection in colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) is one of most common cancer diagnosed worldwide annually. It is a heterogeneous disease and numerous factors such as environmental, genetic, epigenetic, infection, inflammation as well as intestinal microorganisms are involved in CRC onset and progression. Gut bacteria have a critical role in the biological microenvironment and prolonged bacterial infection is associated with colonic tumourigenesis. Mucosa-associated microbiota such as Escherichia coli are mostly identified in colonic tissue of CRC patients. This review summarized the possible pathways involved in colorectal carcinogenesis of E. coli.

Methods: The MEDLINE, Embase, and Cochrane database were searched from 2010 to 2020 and English relevant articles were selected for review.

Results: Tumor-infiltrating Macrophages, contribute to the main steps of carcinogenesis through secreting multiple factors including COX-2/PGE2. The protumoral function of COX-2/PGE2 is influenced by tumor microenvironment. Colon cancer-associated E. coli promote intestinal inflammation and protumoral activities of macrophages by inducing persistent cyclooxygenase-2 (COX-2) expression. Indeed, the association of E. coli with pro-inflammatory infiltrates may increase tumor growth. Mucosally adherent E. coli may also contribute to the colorectal neoplasia progression by downregulating mismatch repair proteins such as MSH2 and MLH1, that are involved in DNA damage associated apoptotic signaling and protecting cells from mutations. Furthermore, cancer-associated E. coli able to produce colibactin, a genotoxin with oncogenic potential.

Conclusion: E. coli may play critical role in colorectal cancer progression via different mechanisms. Additional studies will determine the precise role of E. coli in colorectal tumourigenesis which may be used therapeutically.

Keywords: Escherichia coli, Colorectal, Cancer, Gut, Microbiota

Role of miR-138 in drug resistance and signaling pathway of different types of cancer (Review)

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Introduction: MicroRNAs (miRNAs) are endogenous small non-coding RNA molecules (19-22 nucleotides in length) that regulate the expression of target genes either through translational inhibition or destabilization of mRNA by direct interaction with the 3′untranslated regions (3′-UTRs) of target mRNAs. Notably, due to miRNAs crucial roles in controlling diverse metabolic and cellular biological processes, aberrant their expression could potentially develop into cancers. MiR-138 originates from two primary transcripts, pri-miR-138-1, and pri-miR-138-2 as encoded on chromosomes 3 (3p21) and 16 (16q13), which form the mature miR-138. Changes in miR-138 expression can affect cell proliferation, apoptosis, invasion, metastatic ability, and drug resistance of numerous cancer cells. Besides, miR-138 has been expressed at a low level in many types of human cancer and could function as a tumor suppressor by negatively regulating oncogenes. Interestingly, it was observed only in brain tumors that miR-138 could function as an oncogenic miR in a certain type of brain tumor cells. Moreover, downregulation of miR-138 is involved in the chemoresistance of several cancer types, including prostate, gastric and non-small cell lung cancer, multiple myeloma, renal cell carcinoma, and osteosarcoma. MiR-138 could induce apoptosis and reverse drug resistance of cancer cells by targeting multiple genes involved in multiple processes such as drug transport, drug metabolism, DNA repair, cell survival, and apoptosis. Overexpression of miR-138 in cancer cells could significantly enhance their sensitivity to apoptosis and cell death induced by chemotherapeutic drugs. Besides, it might potentially be used as a combination therapy agent with other therapy methods. Mirna-138 is involved in the pathogenesis and chemoresistance of cancers by directly targeting several mRNAs such as FAK, GPR124, ERCC1, ERCC4, vimentin, H2AX, EZH2, EGFR, K2, and BIM. This article reviews the expression and functional role of miR-138 in various human cancers with its target genes and pathways in a hope to find a better therapeutic option to treat human cancers and highlights potential therapeutic targets for reversing miRNA-mediated drug resistance.

Methods: Original articles and different databases such as PubMed and Google Scholar have been used to write the present review article.

Results: Evidence supports that miR-138 acts as a tumor suppressor and regulates various downstream effectors associated with cancer. However, the oncogenic role of miR-138 was observed in rare cases of brain tumors. The dysregulated miR-138 has been shown to affect the hallmarks of cancer, including sustaining proliferative signaling, evading growth suppressors, resisting cell death, and activating invasion and metastasis. Furthermore, miR-138 affects the chemotherapeutic sensitivity of several human cancer types. More importantly, accumulating evidence has shown that miR-138, as other miRNAs, can regulate multiple targets in can¬cer cells. These findings make miR-138 as an attractive therapeutic option to treat human cancers.

Conclusion: The growing knowledge about the miR-138 impact on several aspects of carcinogenesis and its meaning for therapeutic usage implicates miR-138 to be a promising candidate for response prediction, control, and modification of conventional and/or new developed anticancer treatments. Thus, it is hypothesized that a replacement treatment with miR-138 mimics could be a promising strategy for cancers characterized by downregulation of miR-138. However, there is a need to develop more efficient delivery systems. More important, several studies demonstrated that miR-138 could successfully modulate the sensitivity of cells to well known chemotherapeutic agents. These data point out the immense prospect of using miR-138 in combination with existing therapeutic strategies to maximize the effect of cancer treatment and to improve the survival of patients. Further studies are required prior to implementing miRNA-based cancer therapeutic strategies into clinical practice.

Keywords: MicroRNA; Gene regulation; Apoptosis, Metastasis

Rutin via Increase in the CA3 Diameter of the Hippocampus Exerted Antidepressant-Like Effect in Mouse Model of Maternal Separation Stress: Possible Involvement of NMDA Receptors (Research Paper)

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Introduction: Rutin is a flavonol with neuroprotective activity. The aim of the present study is to investigate the role of the glutamatergic system in the antidepressant-like effect of rutin in a mouse model of maternal separation (MS) stress focusing on histological changes in the CA3 area of the hippocampus.

Methods: Mouse neonates were exposed to MS paradigm 3 hours daily from postnatal days (PND) 2 to 14. The control and MS mice were divided separately into 16 groups (n=8) (8 groups for each set) including mice that received normal saline, mice that received rutin at doses of 10, 50, and 100 mg/kg, mice that received NMDA at a dose of 150 mg/kg, mice that received ketamine (NMDA antagonist) at a dose of 0.25 mg/kg, mice that received NMDA antagonist plus a subeffective dose of rutin, and mice that received NMDA plus an effective dose of rutin. Forced swimming test (FST) was performed. Afterwards, the hippocampus was evaluated in cases of histopathological changes as well as expression of NR2A and NR2B genes.

Results: Rutin significantly reduced immobility time in the FST. The expression of NR2A and NR2B subunits of NMDA receptor in MS mice was significantly higher than that in the control group. Rutin significantly decreased the expression of NR2B and NR2A subunits in the hippocampus. The CA3 diameter and percentage of dark neurons in the hippocampus of MS mice significantly decreased and increased, respectively, which partially reversed following rutin administration.

Conclusion: Rutin, partially, through a neuroprotective effect on the hippocampus exerted antidepressant-like effect. We concluded that NMDA receptors, at least in part, mediated the beneficial effect of rutin.

Keywords: Depression, Hippocampus, Maternal separation stress, Rutin, NMDA

Safety needs of hospitalized elderly patients (Review)

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Introduction: Safety is a major problem when working with or taking care to older patients. There are several safety issues that should be considered regarding with the elderly patients. One of the most important safety subject is ‘‘geriatric syndromes or medical errors,’’ which include falls, delirium, pressure ulcers and underfeeding. Geriatric syndromes are associated with high mortality

Methods: : In the following review article after searching key words “Safety needs ,hospitalized ,elderly patientss” in credible English and Persian databases such as PubMed, Scopus Magiran, Scientific Information Database, web of science and google scholar; until the year 2020 without a date limit, a total of 104 papers were found. After a stepwise and more precise review, 15 papers were selected that were aligned with the purpose of the review study at hand.

Results: The incidence of unintentional injury, which usually results from a fall, assumes among the peak 6 reasons of death in elderly people. The incidence of delirium in hospitalized elderly patients is associated with mortality rates of 25% to 33%. Also, the mortality rate for residents with pressure ulcers in long term care facilities reported 26% over a 6-month follow-up period. Underfeeding is also related with poor clinical outcomes and high mortality. In addition, errors are a vital safety practice that should be considered in geriatric care. The literature identified and extended on six particular recommendations that we believe will improve the safety of geriatric care. These six recommendations consist of the detection and reporting of geriatric syndromes, identifying system failures when geriatric syndromes occur, establishing dedicated geriatric units, improving the continuity of care, decreasing adverse drug effects, and promotion of geriatric training programs

Conclusion: . Elderly people seem to be a special at risk group for medical errors. It is hospitals' responsibility to keep patients safe and considers the significance of safety during their work.

Keywords: Safety needs , hospitalized ,elderly patients

SARS-CoV-2 Receptors: potential therapeutic targets against COVID-19 (Review)

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Introduction: The recent emergence of a novel coronavirus (SARS-CoV-2) in China has caused significant public health concerns. Cell entry is the first and a key step in viral life cycle which its understanding provides functional information on pathogenesis and potential therapeutics of COVID-19. Angiotensin-converting enzyme 2 (ACE2) which was known as receptor for SARS-CoV, is reported as an entry receptor for SARS-CoV-2, recently. The aim of present study is to have an overview on SARS-CoV-2 receptors and its role in host range, pathogenesis, and therapeutic targets to fight the disease and save lives.

Methods: This study was a narrative review performed in 2020 to investigate angiotensin converting enzyme-2 as the receptor of SARS-CoV-2 and antiviral therapeutic strategies. We searched four keywords in six databases including PubMed, Scopus, Science Direct, Web of Science UpToDate, and Google scholar to determine the related documents on the main objective of the study.

Results: A review of current studies revealed that Receptor Binding Domain (RBD) of SARS-CoV-2 has a stronger avidity to ACE-2 compare to SARS-CoV because of key residue substitution in CTD of S protein. In addition to higher affinity of SARS-CoV-2 spike to ACE2, other properties of S protein including priming by serine protease TMPRSS2, furin pre-activation, and hidden RBD in the spike potentially allow SARS-CoV-2 to maintain efficient cell entry via ACE2 and efficient evading from immune response. ACE2 is expressed in various human tissues in addition to the lungs such as gut, kidneys, cardiovascular system, and central nervous system which could intensify virus pathogenesis in multi-organ dysfunction. Intriguingly, based on a prediction model, Glucose Regulated Protein 78 (GRP78) introduced in SARS-CoV-2 entry as a receptor. Indeed, all the above mentioned roles of ACE2, GRP78 and TMPRSS2 has encouraged the researcher to target them as an antiviral therapeutic against COVID-19. Five main strategies are proposed to block the SARS-CoV-2 entry step: 1) targeting viral spike protein; 2) targeting the specific viral receptors including on the host cell surface; 3) applying soluble (s) ACE2 which can bind to S protein to neutralize virus entry; 4) blockage of GRP78; and 5) TMPRSS2 inhibition.

Conclusion: Receptor recognition by SARS-CoV-2 is antiviral therapeutic strategies for tackling the COVID-19 Pandemic. The results of our review indicate that ACE2 might be one of the main contributors in severity and fatality of COVID-19 in human populations. Therefore, blockade of ACE2 and TMPRSS2 inhibition might efficiently inhibit SARS-CoV-2 cell entry and pathogenesis. future studies on

receptors are required to find novel target on prevention and treatment of SARS-CoV-2 pandemic regarding the virus-receptor interaction.

Keywords: COVID-19, SARS-CoV-2, ACE2, GRP78, antiviral therapeutics

Screening of extended-spectrum β-lactamase-producing klebsiella bacteria isolated from Clinical and Microbiological sample (Research Paper)

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Introduction: ESBLs stand for Extended-Spectrum β-lactamase which are enzymes produced by some bacteria and make them resistant to some antibiotics. They can hydrolyze third- and fourth-generation of cephalosporins and monobactams, but not cephamycins or carbapenems. the ESBLs produced by Klebsiella pneumoniae is an important clinical concern in the worldwide. Klebsiella spp, especially Klebsiella pneumoniae and Klebsiella oxytoca, are the most common pathogens causing pneumonia, meningitis, urinary tract infections and bloodstream infections. Klebsiellae have developed resistance to a wide range of antibiotics such as aminoglycosides, cephalosporins and wide range of β-lactams, including carbapenems, and have posed serious problems in antibiotic management with limited treatment options. The aim of this study was to identification and screening of the beta-lactamase producing Klebsiella.

Methods: In this study, a cross-sectional descriptive-analytical study was conducted over a period of 3 months. 36 specimens of Klebsiella were identified by biochemical-differential methods collected by culturing of urine, blood, secretions and sputum. Isolates were tested for antibiotic susceptibility. Phenotypic identification of 35 klebsiella isolats for ESBL production was confirmed by double disc synergy test, phenotypic confirmatory double disc test. The seven isolates with ESBL phenotype were sequenced by 16SrRNA molecular identification method.

Results: Among 36 Klebsiella isolates, 15 isolates (41.6%) produced ESBL. Antibiotic resistance in beta-lactamase-producing bacteria against ceftazidime, cefotaxime, and cefixime (92.8%) was higher than other antibiotics. Among the resistant isolates, the major identified species were Klebsiella Pneumoniae (71.42 %), Klebsiella oxytoca (14.27 %), Klebsiella quasipneumoniae (14.27 %).

Conclusion: Based on this study and sequencing of Klebsiella isolates, Klebsiella pnemoniea the most resistant isolated species against a wide range of antibiotics.

Keywords: Extended-spectrum b-lactamases (ESBL), Klebsiella bacterium, Antibiotic resistance

Screening of Large Neutral Amino Acid Transporter 1 (LAT-1) Inhibitors Using FOOD-lib Library and Lipinski's Rule (Research Paper)

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Introduction: SLC7A5, known as L-type Amino acid Transporter 1 (LAT1), belongs to the APC superfamily and forms a heterodimeric amino acid transporter interacting with the glycoprotein CD98 (SLC3A2) through a conserved disulfide [1]. LAT1 is a membrane transport protein that preferentially transports branched-chain (valine, leucine and isoleucine) and aromatic (tryptophan, tyrosine) amino acids [2]. LAT1 plays a significant role in the growth and propagation of cancer cells by facilitating the cross-membrane transport of essential nutrients, and is an attractive drug target [3]. Here, we report a structure-based approach to identify chemically diverse and potent inhibitors of LAT1.

Methods: At first, the three-dimensional (3D) structure of the LAT-1 was downloaded from RCSB (PDB ID: 6JMQ/Chain A). In order to virtual screening, a library containing 10997 compounds (FOOD-lib) was used in MTiOpenScreen server. Virtual screening against the LAT-1 was performed by using AutoDock Vina program. Ligands with less than -10 binding energy were selected for subsequent analysis. The molecular structures of ligands were analyzed using SWISSADME server in order to confirm whether the physicochemical properties like molecular weight, hydrogen bond donor, hydrogen bond acceptor, lipophilicity and molar refractivity of ligands follow Lipinski's rule of five or not. Absorption, distribution, metabolism, and excretion (ADME) each profile of ligand was calculated using pkCSM server. General toxicity, cardiotoxicity (Pred-hERG server) and hepatotoxicity (Vienna LiverTox server) were investigated. Metabolism sites of best ligand to three isoforms i.e. CYP3A4 CYP2D6 and CYP2C9 of cytochrome P450 family of enzymes were predicted utilizing online-based RS-WebPredictor server.

Results: After docking, 12 top ligands were chosen (Energy < -11). Two ligands followed Lipinski's rule. Toxicity of these two ligands was investigated, and finally, Smilagenone (ZINC000118936408) was found to be non-toxic, and its cytochromes P450 metabolism sites were determined.

Conclusion: Given the role of LAT1 in cancer progression, LAT1 was selected as a drug target. Virtual screening on MtiOpenScreen server identified 12 drug candidates. After pharmacokinetic and pharmacodynamic studies, composition Smilagenone was selected as the lead compound. It is expected Smilagenone will act as an inhibitor and prevent the supply of amino acids to cancer cells, thus impeding the protein synthesis and cellular proliferation. Authors suggest further in vitro and in vivo study with Smilagenone to confirm their anticancer activities and strengthen this finding.

Keywords: AutoDock Vina, Cancer, LAT1, MTiOpenScreen, SLC7A5.

Simulation of the inhibitory effect of common antiviral drugs on Spike glycoprotein for the treatment of infections caused by Covid19 (Research Paper)

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Introduction: Coronavirus is a type of enveloped viruses and it has a size of about 120 to 160 nm and contains a single strand RNA genome fragment and it is known as one of the largest RNA viruses. Coronavirus consists of four genera: alpha, beta, gamma and delta, and tow genera alpha and beta cause disease in humans. At the beginning of the new year (2020), the Coronavirus caused a global epidemic that has so far spread to more than 200 countries and more than 24 million people worldwide have been infected with Covid 19 disease; and More than 800,000 people around the world have died from modern coronavirus infections; And because of extensive genomic changes,in this virus, So far, no effective vaccine or drug has been introduced for it. Covid 19 belongs to the class of beta-coronaviruses. On the outer surface of the virus coat, there are stick-shaped protrusions about 20 nanometers long that create a sun-like appearance and act as the virus-binding protein to its receptor in lung tissue, and called the spike glycoprotein. To be Studies have shown that the ACE2 protein is a coronavirus receptor, and for coronavirus pathogenic function, it must first bind to the receptor in lung, esophageal, epithelial, and colon cells. Connect. After binding of Spike glycoprotein to its ACE2 receptor, the virus protein is broken down by proteolysis by catepsin or furin proteinase, and the virus coat fuses with the cell membrane. Common symptoms of Covid 19 infections include fever, fatigue, muscle aches, cough, and shortness of breath, and myocarditis, diarrhea, and vomiting are rare. The aim of this study was to introduce the best inhibitor through molecular interaction between spike protein and existing antiviral drugs.

Methods: The sequence of Spike SARS2(surface glycoprotein [Severe acute respiratory syndrome coronavirus 2]) with Accession: QJX59884.1 was retrieved from NCBI website (www.ncbi.nlm.nih.gov/protein) in FASTA format. The modeling and energy minimization experiment were performed on SWISS-MODEL server (https://swismodelexpacy.org) and From Five models extracted here the best one was selected based on RAMPAGE analysis(https://servicesn.mbi.ucla.edu/PROCHECK/) and used for further experiments. This structure then refined for blind docking experiments in HEX (version 8.0.0). The docking experiments were done using 60 different available antiviral drugs to study their interactions and to survey their bind sites. Coordinate structures of 60 antiviral drugs were designed in .PDB format with ChemDraw Professional 15.0 software and optimized in ArgusLab. software. Docking results were analyzed in ArgusLab, PyMOL, LigPlus and WebLab Viewer softwares and finally Evaluation of the toxicity effect of selected drugs were performed on adverpred server (http://www.way2drug.com/adverpred/).

Results: Spike protein simulation showed that this protein has three chains A, B and C, and each chain of this protein contains 1147 amino acids, and the first amino acid is Ala27 and the last amino acid is Ser1147, and 26 amino acids are in the N-terminal caudal region. The results of molecular docking of drugs and Spike protein showed that Ampligen, Atazanavir, Cobicistate, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Remdesivir, Ritonavir, Telaprevir and Tripranavir have higher and more favorable negative binding energy and better connected to the protein binding site. The results of this study showed that Spike glycoprotein has a binding site in all three subunits, and the amino acids Arg1968, Cys1972, Ala1973, Lys1975 and Phe1976 are common binding sites of selected drugs and Remdesivir binds to subunits A and C.

Conclusion: Spike glycoprotein after binding to its receptor, it is broken down by the enzyme proteinase into two subunits S1 containing the Protein binding domain and subunit S2. The results of this study showed that Atazanavir, Cobicistate, Indinavir and Lopinavir by binding to the Spike protein and restrain it, inhibits the enzymatic break down of this glycoprotein and prevent the S1 subunit from binding to its receptor in the cell.

Keywords: Spike, Covid19, Lopinavir, Binding site, ACE2

Sleep Duration in Association with Oxidative Stress and Anxiety/Depression (Research Paper)

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Introduction: From an evolutionary point of view, sleep is a vital behavior for human beings. It has been demonstrated that sleep is closely associated with metabolic, psychiatric, cardiovascular, and immune system disorders. Nowadays, there are some controversies on the association between sleep duration, oxidative stress determinants, and the severity of anxiety and depression. Thus, in this study, we have decided to investigate their relationship in a cross-sectional analysis of a populated metropolis in the middle east region.

Methods: As a part of the Mashhad Stroke and Atherosclerotic Disorders (MASHAD) cohort, 9184 subjects were included in our cross-sectional study. Sleep duration was recorded within a complete 24 hours using a self-report questionnaire. After excluding night shift workers, subjects were divided into very short sleep (<5h), short sleep (5-7h), and normal sleep (>7h) subgroups based on the duration of their nocturnal sleep. Pro-oxidant/antioxidant balance (PAB) and superoxide dismutase enzyme (SOD1) activity were measured for all subjects by standard methods. Beck anxiety inventory (BAI) and Beck depression inventory (BDI) questionnaires were used for anxiety and depression assessment; 0-13, 14-19, 20-28, and 29-63 scores of BDI were classified as minimal, mild, moderate, and severe depression, respectively. In addition, the following classification was used for anxiety according to BAI: minimal (0-7), mild (8-15), moderate (16-25), and severe (26-63). SPSS version 18.0 was used for performing statistical analysis with consideration of p-value under 0.05 as significant.

Results: In a crude model, our analysis found a substantial difference in PAB and depression and anxiety scores between subgroups of sleep duration. These factors were significantly higher in the very short sleep subgroup than the others. By Multivariate Analysis Of Variance (MANOVA), our results showed that just in anxious subjects, PAB level decreased by 10.721 and 11.690 HK in the short and normal sleep subgroup than the reference one (very short sleep). In addition, our analysis revealed that nocturnal sleep duration is considerably lower in severe depression and anxiety subjects than the others. Moreover, minimal anxiety and depression participants had a significantly lower level of PAB than the other subgroups of anxiety and depression severity.

Conclusion: Our cross-sectional study on a large sample of Mashhad citizens proved that nightly sleep deprivation (<5h) is substantially associated with increased PAB and severe depression and anxiety. Besides, PAB level was

significantly related to the severity of anxiety and depression; However, SOD1 was not significantly associated with nocturnal sleep duration and depression/anxiety. More clinical cohort and case-control investigations are to clearly demonstrate the exact direction of these associations.

Keywords: Sleep; Sleep deprivation; PAB; Anxiety; Depression

Sponge Dysidea Avara induction of ROS mediated apoptosis in human glioblastoma cells via mitochondrial targeting (Research Paper)

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Introduction: Glioblastoma is the most lethal brain tumor with poor prognosis which possesses a high resistance against anticancer drugs. Marine organisms are an abundant source of bioactive molecules. Different studies on marinesponges indicated that sponge Dysidea avara, have cytotoxic effects on cancer cell lines; therefore it is suggested that marine drugs can potentially be used as a beneficialmedicine in cancer therapy. Sponge Dysidea Avara's anti-cancer effects and associated mechanisms were assessed in brain tissues, focusing on parameters of inflammatory change and apoptosis.

Methods: Mitochondria were isolated from the glioblastoma cells by mechanical lysis and multiple centrifugations. The activity of mitochondrial complex II was assayed via the measurement of MTT reduction. The mitochondrial ROS measurement was performed using the fluorescent probe DCFH-DA. The Rhodamine 123 (Rh 123) redistribution technique was used for MMP measurement. Mitochondrial swelling was measured spectrophotometrically in duration 1 hour. Caspase-3 activity was evaluated using the Sigma caspase-3 assay kit. Data were analyzed using the Graph pad prism software, version 7.

Results: Our results demonstrated that Dysidea Avara induced a rise in mitochondrial reactive species (ROS) formation and mitochondrial membrane potential (MMP) collapse before mitochondrial swelling ensued in isolated brain mitochondria. In addition collapse of MMP and mitochondrial swelling produced release of cytochrome c via outer membrane rupture or mitochondrial permeability transition (MPT) pore opening. Furthermore, caspase-3 activity was significantly increased in cells isolated from the brain when incubated with Dysidea Avara.

Conclusion: The present study concluded that Dysidea Avara could be a potential anticancer agent. However, additional studies are needed to clarify involved mechanisms.

Keywords: Apoptosis, Dysidea Avara, Glioblastoma, Mitochondria

Stem Cell Therapy As A Therapeutic For Congenital Heart Disease Treatment: A Review of Animal Model Studies (Review)

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Introduction: Congenital heart disease (CHD) is the most common birth defects and cause of infant death in the world. Currently, surgery is the gold standard treatment choice for CHD but The risk of postoperative ventricular dysfunction increases as children grow older and the chance of heart failure due to repeated interventions and surgeries amplifies. Stem cells(SC) are none specialized cells that can differentiate into other types of cells. Embryonic stem cells, induced pluripotent stem cells, mesenchymal stem cells, adipose-derived stem cells, umbilical cord blood cells, amniotic fluid-derived stem cells are types of stem cells can use for therapeutic goals. In this study, we investigated the role of SC therapy in congenital heart disease.

Methods: A comprehensive search was conducted in electronic databases Pubmed, Scopus, Web of Science, Science Direct and Google Scholar with the keywords “stem cell” and “congenital heart disease” since 2008. Animal studies were included. Review studies were excluded.

Results: from 15 studies, 7 articles were selected according to the including and excluding criteria. The animals have been studied include, New Zealand white rabbits, Pregnant Border Leicester sheep, Adult Sprague-Dawley rats. In piglets with right ventricle and the pulmonary artery disorder, thymus-derived mesenchymal, intracoronary stem cell, perinatal stem cell-derived vascular smooth muscle cells and human embryonic stem cell–derived cardiac progenitors, in sheeps with right ventricle disorder, human cord blood stem cells, in rabbits with Hyperkinetic pulmonary arterial hypertension, endothelial progenitor cell and in rats with right ventricle disorder, Mesenchymal Stromal Cells were transplanted. According to studies, stem cells can have a therapeutic effect on congenital heart disease. There are also few side effects of this treatment.

Conclusion: , regarding the above mentioned studies, stem cell therapy in congenital heart disease is safe and has some benefits. Although this treatment

method doesn't have current complications of the surgery, it is not sufficient and It should be used in combination with other therapeutic interventions. Therefore, further studies should be performed to identify complementary interventions with stem cell therapy as well as existing ambiguities.

Keywords: Animal, Congenital Heart Disease, Stem cell, Surgery

Stem Cells Against Liver Cirrhosis: A systematic Review of Randomized Controlled Trial Studies (Review)

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Introduction: Introduction, Liver cirrhosis is an end-stage of liver damage condition which is a common cause of death in the world. Today liver transplantation is only a therapeutic option for the patients, but the lack of donor and transplantation rejection are several obstacles for cirrhotic patients. Stem cells are non-specialized cells that can differentiate into specialized cells. The embryonic, adult, induced pluripotent, cord blood and amniotic fluid are types of stem cells that can use for different therapeutic goals. In this study, we investigated the role of SCs in liver cirrhosis treatment.

Methods: Materials & Methods, A comprehensive search was conducted in electronic databases Embase, Pubmed, Scopus, Web of Science and Clinical Key with the keywords “stem cell” and “liver cirrhosis” since 2012. Randomized controlled trial studies were included. Review of RCT studies were excluded.

Results: Results, Of 148 studies, 15 articles were selected according to the including and excluding criteria. Several types of stem cells like mesenchymal stem cells, hematopoietic stem cells, liver progenitor cells, induced pluripotent stem cells, and bone marrow mononuclear cells have been investigated as a possible source of liver regeneration. According to studies, the therapeutic effects of stem cells on cirrhotic liver recovery depend on the type of stem cells, the source of stem cells and the cause of liver cirrhosis. These variations have been caused by different effects, whether therapeutic or non-therapeutic, on patients received stem cells. What is more likely is that autologous stem cell transplantation might have more effective effects on liver regeneration. Although stem cell transplantation has various therapeutic effects, on the other hand, this method of regenerative medicine has fewer complications in comparison with liver transplantation.

Conclusion: Conclusion, due to the mentioned studies, stem cells for the treatment of hepatic cirrhosis are not currently applicable and safe at present. Although stem cell transplantation doesn't have current complications of liver transplantation,

instead the clinical efficacy of this therapeutic method did not prove yet. So more studies are needed in this field to clarify ambiguous subjects.

Keywords: Keywords: Liver cirrhosis, Liver transplantation, Stem cell

Strategies for preventing mother-to-child transmission of htlv1 infection (Review)

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Introduction: htlv1 is an infection that infects lymphoid T cells in humans. One of the main ways of transmitting is the mother to the child, especially through breastfeeding. Knowing how to prevent the transmission of this disease can be considered important. This review study was conducted to summarize the strategies for preventing the disease and to find the basis for its effective prevention.

Methods: By searching for keywords in google scholar and pubmed databases, 22 and 14 articles were compiled between 1998 and 2017. By reviewing the title of the articles, 23 articles were omitted due to lack of consideration of this issue and discuss about other issues. Subsequently, by reviewing the abstracts of the remaining articles, 6 articles were selected and 7 articles were deleting due to the case report studies and case series studies

Results: short_term breastfeeding (less than 6 months) strategy was examined. The transmission percentage decreased from 20.3 to 2.5. 2. milk of mothers with HTLV-1 was frozen at _20. Other viral antigens were not detected in breast milk. 3. to worm the milk of mothers with HTlV-1 to 56 for half an hour. Other viral antigens were not detected in breast milk. 4. cesarean section was preferred to normal delivery since the percentage of transmission in normal delivery was %2.7 higher than the cesarean section. 5. combination of two drugs, Zidovudine and Valproic Acid, which caused a significant reduction in viruses in mothers with HTLV-1. Recommended the use of this method during delivery and later delivery. 6. to use Zidovudine during labor and during pregnancy as it was investigated that %2.5 of infants who were only breastfeeding were tested for HTLV-1 antigen. This indicates intrauterine transmission or delivery.

Conclusion: we found in this study and the others that the prohibition of breastfeeding could be an effective way of preventing mother-to-child transmission of htlv1.

Keywords: prevention, transfer, htlv1

Structural and mechanical analysis of decellularizing rabbit kidney using SDS and SDS-Triton as detergents (Research Paper)

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Introduction: Tissue engineering is a multidisciplinary field that uses engineering, materials, and cells in restoring tissue functionality. Scaffolds play the role of ECM so they should have the biological and structural features of the original tissue. Recently the use of decellularized tissues as a natural scaffold has been studied. Decellularization is the process of isolating cells from an ECM that leads to a scaffold. Acellular ECM is the most mimetic scaffold to the natural ECM in engineering different tissues, including ligament, tendon, etc. Various methods have been proposed for tissue decellularization. Triton X100 and SDS are the most common nonionic and ionic detergents. Tissue differences need optimization of the decellularization method according to the tissue in a manner that does not harm the main components of the ECM. Recently, some researches aimed to investigate the effects of different decellularization protocols on ECM structure and composition. In this paper, rabbit kidneys have been decellularized by SDS and SDS-Triton perfusion. Then the two protocols compared by using fluorescence staining, calculating the remaining DNA, and determining mechanical properties

Methods: Decellularization Rabbit kidneys were connected to a peristaltic pump by cannulation through the renal artery. The first group perfused using SDS 2% for 96hr. The other group first perfused with SDS for 94hr and then perfused with Triton X100 for further 2hr. Optical microscopy samples, sliced with 3mm thickness (for formalin diffusion) and fixed in 48hr. Then the samples dehydrated using a series of increasing alcohol concentration paraffinized and sliced into extremely thin slices using a microtome. H&E and DAPI staining are used for histology and labeling DNA and evaluating decellularization process respectively. Glutaraldehyde (Merck) is used for fixing tissues for electron microscopy. Then samples dehydrated, dried using freeze drier for 24h and coated with gold to be conductive. Compression testing with a 50% deformation was used for determining the mechanical properties of the decellularized tissue.

Results: SEM images show the scaffold structure. The images show that cell removal leads to pores with a size of around 75 microns. Also, it is seen that Different parts of the kidney have their characteristic topography. DNA staining reveals that using SDS and Triton simultaneously as a decellularization agent leads to less DNA content in comparison to SDS. H&E staining figures of the normal kidney are representative of proximal and distal tubules, bowman's capsule and glomerulus. Also, it can be seen that in both of the protocols the structure of the basic components of the kidney is well preserved in comparison to the normal kidney. Triton-SDS processed scaffolds have the least DAPI staining which shows the maximum cell and debris removal.

Conclusion: H&E staining shows that SDS and SDS-Triton agents do not change ECM structure seriously and the structure is the same as normal tissue. But comparing DAPI staining reveals that Triton helps to more material extraction from the ECM. Comparing the Compressive strength of the normal and acellular tissue shows that since the cells are harder than the ECM, cell removal causes strength loss. Also, using SDS – Triton resulted in a weaker scaffold than the ECM decellularized using Triton. Based on the above-mentioned results Triton-SDS is considered the most effective strategy for cell removal and structure preservation

Keywords: Natural scaffold- acellular matrix- Tissue engineering - regenerative medicine

Studies of the effects and possible side effects of herbal medicines on breast cancer (Review)

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Introduction: Breast cancer is one of the most common reasons of cancer mortality among women, and apoptosis is an important phenomenon for the destruction of cancer cells. Natural compounds with cytotoxic effects (apoptosis) are considered as potential therapists. In this paper, cytotoxic effects of 3 plants Zofa, Rosemary, and Mycelium on MCF-7 cells and Dana racemosa (hamishak) plants on 4T1 cells are studied and compared.

Methods: MCF-7 cells and 4T1 cells are cultured in RPMI1640 medium with 10% FBS, 5% CO2 and 37 ° C in the presence of different concentrations of plant extracts. To assess the cytotoxic effect of the extract on the cells, the MTT colorimetric method is used and the survival rate of the cells is determined.

Results: The results of the MTT assessment of cancer cells that have been affected by different concentrations of the alcoholic extract of the perennial plant(Hamishak) have shown that it is highly depended on the number of plant cells and time. The results of the MTT test examined the ethereal petroleum extract and the ethyl acetate of the mycelium fungus shows that the effect of the cytotoxicity of ethyl acetate extract on MCF-7 cells was much greater. The effect of nysome containing rosemary essential oil was investigated and it was found that the percentage of cell viability decreased with increasing essential oil concentration, which was proportional to the increase in essential oil concentration. The MCF-7 cells were exposed to the methanolic extract of Zufa flowers, and at the same time, their survival rate was significantly reduced. The bioavailability of the methanolic extract of Zufa also reduced the chances of survival of MCF-7 cells.

Conclusion: this study argued that the methanol extract of Zofa in the lowest quantity among 4 studied plants was able to significantly reduce the chances of survival of MCF-7 cells. Considered of its fast rate and cost-effectiveness of the drug and high potential against MCF-7 cells.

Keywords: MCF-7 Cell Category, 4T1 Cell Category, Cytotoxic Effect, Herbal Extract, MTT Test

Study of frequency and effective factors on depression in caregivers of cancer patients: A review study (Review)

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Introduction: Depression is one of the most common mood disorders that is associated with symptoms such as lack of pleasure, lack of motivation, libido disorders, sleep disorders and depressed mood. This disorder affects all aspects of life. Due to the importance of depression in caregivers of cancer patients, the purpose of this study is to review the frequency and factors associated with depression in caregivers of cancer patients.

Methods: This study was conducted in 1399 with the steps of designing a study question and searching, which was determined through MESH strategy in Google scholar search engine and databases such as SID, PubMed, Science Direct, Scopus using keywords including "Cancer", "Abundance", Depression ", "Caregiver" and "Effective Factors". Relevant studies were then identified from 2007 to 2020. From a total of 143 studies, after screening the title, abstract and full text, 23 studies were selected. Finally, the findings were classified.

Results: The findings of the present study indicate that the range of moderate to severe depression in caregivers of cancer patients is between 22-32.8% and mild depression is between 19-27.4%. Factors influencing depression in caregivers of cancer patients were also divided into three main categories. Individual factors mentioned in 13 studies include: age, education, gender, patient relationship, number of family members, coping strategies, and religious beliefs. The medical factors selected from the four studies included a history of physical and mental illness in the caregiver, the patient's type of cancer, the stage of the disease, and the medications received by the patient. Social factors influencing caring stress include economic status, disease awareness, social support, social class, level of social activity, and hours spent with the patient, as reported in 6 studies.

Conclusion: The results of the literature review show a relatively high frequency of depression in caregivers of cancer patients. Following this study, by identifying the related factors in the frequency of depression, it can be helped to eliminate it

Keywords: Caregivers, Frequency, Depression, Cancer, Effective factors

Study of IL-1 Genes Polymorphisms in HBs-Ag Positive and Normal Population of western azerbaijan province (Review)

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Introduction: Hepatitis B virus (HBV) is the most common cause of acute and chronic liver disease worldwide, especially in Asia and Africa, with an estimated 350 million people worldwide carrying the virus.Currently, hepatitis B is one of the major health problems in our country and approximately 3 to 8% of the population is somehow involved with the disease.

Methods: Genetic studies on multiple carriers have revealed that human leukocyte antigen (HLA (and various cytokine genes such as:)) 4-TNF-alpha, TNF-gamma, IL-12, IL-18, TGF-beta genes , IL-10, IL-1, IL (associated with HBV sensitivity or its durability or disease severity. Cytokines play an important role in defense against viral infection; IL-1 is also one of the cytokines. The most important members of the IL-1 family include IL-1alpha, IL-1beta, and IL-1RN, all of which are polymorphic, which is a major pro-inflammatory factor and plays a central role in inflammation and viral elimination. Polymorphisms are located in gene regulatory regions and have functional significance with They have a strong role in regulating IL-1 protein production and are associated with the spread of certain diseases. Studies in patients with hepatitis B in Japan have found that a link between IL-1beta polymorphisms and cirrhosis associated with hepatitis B Another study in the same country found that polymorphisms of this gene may be associated with predicting the risk of inflammatory diseases. Some studies on the polymorphisms of the ILRN1 gene also suggest that individuals with the 2-intron allele of the IL-1RN gene may be resistant to HBV infection.

Results: There has also been no study of the association of IL-1alpha polymorphisms with this disease. In this project, the polymorphisms of interleukin 1 genes will be compared in two groups, the first group of patients with known HBs-Ag positive virus infection and the second group of completely healthy individuals without a history of anti-hepatitis B vaccine and They have no previous signs of HBs-Ab, HBc-Ab, hepatitis B.

Conclusion: In general, we have shown in this article that the frequency of alleles of HLA antigen genes and different cytokine genes are related to HBV sensitivity or persistence or severity of disease. There is a direct link between IL-1Beta polymorphisms and hepatitis B-related cirrhosis. However, IL-1RN gene polymorphisms are resistant to hepatitis B in people with Aller 2 IL-1RN intron gene.

Keywords: HBV،HBs-Ab،HBc-Ab،TNF،HLA

Study of Immune Cells Involved in the Antitumor Effect of Kefir in a Murine Breast Cancer Model (Review)

Alimohammadi,[1,*]

1.

Introduction: Administration of kefir and a kefir cell-free fraction (KF) to mice injected with breast tumor cells produced, locally in the mammary gland, different profiles of cells secreting cytokines. Here, the immune cell populations in mammary glands affected by the cyclic consumption of kefir or KF for 2 or 7 d were evaluated using a breast tumor model. Apoptosis was also assayed as another mechanism involved in tumor growth delay. The rate development of tumor cells, IgA(+) cells, and CD4+ and CD8+ T lymphocytes was monitored in mammary gland tissues. The number of Bcl-2(+) cells in the mammary gland was compared with the apoptosis observed in the tumor.

Methods: Female BALB/c mice from Charles River Laboratories (Montreal, Quebec, Canada), weighing 19 to 21 g, were separated into 5 experimental groups: 1) a tumor control group,istered this dilution showed the best intestinal immune response without microbial translocation to the visceral organs (Vinderola et al., 2005). The daily intake of kefir was 3.1 ± 0.3 mL/mouse.

Results: Different cytokine profiles were reported for mice injected with the breast tumor cells that received 2 or 7 d of cyclical administration of kefir or KF. This result suggests that oral administration of this fermented product or its cell-free fraction induced the activation of different cells in mammary glands compared with those activated only for tumor injection

Conclusion: The present study allows a better understanding of the mechanisms involved in the antitumor effect observed in mice administered kefir or KF. The importance of an adequately balanced local immune response in the mammary glands to avoid tumor growth was shown. The importance of nonmicrobial components released during milk fermentation and the period of administration needed to obtain beneficial antitumor effects was also reported. Other mechanisms related to estrogen synthesis in the mammary gland could also be involved in the effect observed with kefir administration.

Keywords: kefir

Study of Lactic Acid Bacteria from Iranian Camel Milk (Research Paper)

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Introduction: Camel milk is the most important of dairy foods. It contains amino acids, vitamins, probiotics properties, and a potential source for isolation of probiotic Lactobacillus strains. This study is aimed to identify and isolate the bacteria special Lactic Acid Bacteria in the camel milk based on the molecule methods.

Methods: All samples were collected from camel milk in the Semnan province of Iran. Initially, they were cultivated in MRS Agar. Plates were incubated by 37 °C for 48 hours. Bacteria identification was done according to interior transcription of the area 16 SrRNA. The products of PCR were successfully determined and were analyzed. Finally, a phylogenetic tree was constructed by using Clustal Omega.

Results: The observed bacteria were gram-positive, catalase-negative rods or cocci and vancomycin-resistant. Following that they identified as E. gallinarum and E. casseliflavus by analytical results ribosomal DNA sequencing with 100% similarity. Also, a phylogenetic tree is proven the species relatedness of the Enterococcus spp.

Conclusion: These findings showed that supporting 16S rRNA sequences is a reasonable technique for identifying Lactobacillus strains. Also, isolated bacteria are a strong candidate for using in food and pharmaceutical industry.

Keywords: E.casseliflavus, E.gallinarum, Enterococcus, Probiotic, 16s rRNA

Study of liver in HBV-related hepatocellular carcinoma: Stereology shows quantitative differences in liver structure (Research Paper)

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Introduction: Hepatocellular carcinoma is one of the main consequences of liver chronic disease. Hepatocellular carcinoma-related changes may be seen in patients with chronic hepatitis B. The aim of the current study was to quantitate liver tissue elements by stereological technique in patients with hepatitis B-related cancer and compare the results with control and only hepatitis B group. Needle liver biopsies from 40 patients with only chronic hepatitis B infection, from 41 patients with only early hepatocellular carcinoma, from 40 patients with early hepatitis B-related cancer and 30 healthy subjects (control group) were analyzed by stereological method using systematic uniform random sampling method. Haematoxylin and eosin stained sections were used. The numerical density of hepatocytes, hepatocyte volume, numerical density of Kupffer cells, volume density of the connective tissue in the portal space, and volume density of the connective tissue were assessed. Quantitative analysis of liver samples indicated that there were statistically significant differences in the numerical density of hepatocytes, hepatocyte volume, numerical density of Kupffer cells, volume density of the connective tissue in the portal space, and volume density of the connective tissue between control and hepatitis B-related cancer and hepatitis B groups. Quantitative, stereological technique is simple and reliable for evaluating HCC in chronic hepatitis B. It is useful for assessing the liver tissue parameters. Stereology is recommended for the diagnosis of people prone to cancer in patients with chronic hepatitis B.

Methods: Needle liver biopsies from 40 patients with only chronic hepatitis B infection, from 41 patients with only early hepatocellular carcinoma, from 40 patients with early hepatitis B-related cancer and 30 healthy subjects (control group) were analyzed by stereological method using systematic uniform random sampling method. Haematoxylin and eosin stained sections were used. The numerical density of hepatocytes, hepatocyte volume, numerical density of Kupffer cells, volume density of the connective tissue in the portal space, and volume density of the connective tissue were assessed.

Results: Current study has shown the application of the stereology in diagnosis of HCC susceptible patients with HBV. This method can be used to study the changes in liver tissue when using a new treatment. Also, stereological parameters can follow up patients with chronic hepatitis B. Quantitative analysis of liver samples indicated that there were statistically significant differences in the numerical density of hepatocytes, hepatocyte volume, numerical density of Kupffer cells, volume

density of the connective tissue in the portal space, and volume density of the connective tissue between control and hepatitis B-related cancer and hepatitis B groups. Quantitative, stereological technique is simple and reliable for evaluating HCC in chronic hepatitis B.

Conclusion: Consequently, stereology is a simple and reliable quantitative technique for the measurement of liver elements such as the number of hepatocytes and Kupffer cells and volume density of the connective tissue in different aria of the liver in patients with chronic hepatitis B. Also, it can assess the fibrosis in biopsy specimen. We recommend this method as one of the most important tools for follow up of patients because it has a high reproducibility in intra field assessment and low intra observer variability. We hope that the results elicited by the present study can be translated into improving the diagnosis conditions for populations worldwide, especially for those individuals living in poor and developing countries.

Keywords: Hepatocellular carcinoma, hepatitis B, stereology

Study of the Effect of Green Algae Extract on the Propagation of Human Mesenchymal Stem Cells on Electrospun Nanocomposite Scaffold (Research Paper)

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Introduction: Nanocomposite electrospun fibers containing bioactive molecules, which offer the ability to deliver the cells into the damaged organs, will help to achieve a high therapeutic effect and enable a wide range of manipulations in the field of reconstructive medicine research. In this study, Alcoholic extract of blue algae afanizomenon flus-aqua (AFA) was used to improve the performance of electrospun polycaplactone (PCL) and gelatin (gel) scaffolds to enhance the survival and proliferation of human mesenchymal stem cells.

Methods: For this purpose, polycaprolactone / gelatin nanocomposite porous scaffolds were prepared using electrospinning method. The constructs were characterized for structural, mechanical and biochemical properties. The nature of human mesenchymal stem cells was confirmed by bone differentiation and flow cytometric analysis. Four culture groups: Two groups without scaffold (to investigate the effect of extract alone) and two culture groups on scaffold (to investigate the synergistic effect of AFA extract on scaffold) were designed. Electron microscope images were used to examine cell attachment on designed scaffold. Cell viability and proliferation in each groups were determined by MTT assay.

Results: The results showed that the biocompatibility and biodegradability of the scaffold with good structural properties such as shape uniformity, pore size and porosity. After 72 hours of culture, the rate of cell attachment and proliferation was significantly higher in the scaffolding groups than others ($P < 0.05$). In alcoholic extract groups, the rate of survival and cell proliferation after 72 hours of culture increased significantly ($P < 0.05$).

Conclusion: In term of the capability of natural nanocomposite scaffold and hMSCs in cytocompatibility analysis, this novel tissue-engineered construct could be suggested as a body substitute to repair injured organs and regenerative medicine application.

Keywords: : Mesenchymal stem cells, nanocomposite, electrospinning, poly caprolacton, Gelatin, Natural compoun

Study of the Electrospun Nanocomposite Scaffold effect on propagation of Human Spermatogonial Stem Cells (Research Paper)

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Introduction: The process of spermatogenesis in humans is complex and unknown, and spermatogonia stem cells are important because of their role in transmitting hereditary information. Efforts to provide a body-like environment for various research and therapeutic purposes have always been considered. In this study, the culture system on the electrospun polycaprolactone / gelatin scaffold was evaluated for its efficiency in the proliferation of human spermatogonial stem cells.

Methods: For this purpose, nanocomposite porous scaffolds were prepared using electrospinning method and their structure was confirmed using scanning electron microscope (SEM) and Characterization methods. Isolated human spermatogonial stem cells (SSCs) were cultured on designed scaffolds and their viability and proliferation during two weeks of culture were compared with the control group.

Results: SEM studies showed that the resulting porous scaffold had suitable diameter and arrangement. The scaffold was biocompatible and biodegradable. Also, Studies on cell activity and proliferation showed a significant increase in the number of spermatogonia stem cells in the scaffold culture group compared with the control (P 0.05). Immunocytochemical findings confirmed the presence of human spermatogonia stem cell colonies in cultural groups.

Conclusion: Overall, the resulting electrospun scaffold seems to provide a suitable capacity for self-regeneration of human spermatogonia stem cells and could have a good application potential for use in research and clinical regenerative medicine of male infertility.

Keywords: Spermatogonia stem cells, polycaprolactone, gelatin, electrospinning

Study of Venlafaxine Effect on Development of the Brain and Expression some of the Related Genes in the Mouse Embryo (Research Paper)

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Introduction: Depression is the most common mood disorder in today's society. It is twice as common in women as in men and is the first onset of depression in a woman's reproductive years. Depression can have many side effects if not treated in women before or during pregnancy. Taking antidepressants is not the right choice because it may cause brain disorders in the fetus. There are few antidepressants that have been shown to be safe to use during pregnancy and lactation, one of them is Venlafaxine. Few experimental studies have been performed on this drug and it may cause neurological and brain disorders in fetuses and infants, as well as the individual. Therefore, in this experiment, the effect of Venlafaxine on the differentiation of mouse fetus brain and the expression of three key genes affecting brain development has been investigated.

Methods: In this study, two groups of 7 balb/c rats were used. one group was treated with 35mg/kg Venlafaxine before pregnancy until 20 days after birth. brain tissue samples were taken using dissection. Then the brain size of the mouse embryos was evaluated using Image j software. Finally, brain tissue RNA was extracted from the target tissues, then their cDNA was synthesised and the expression of TUBB5, DDC, SHANK3 genes were measured using Real Time PCR technique. To analyze the expression of genes, Rest 2009 software was used and the gene network of these three genes was plotted using cytoscape software.

Results: results showed a significant increase in expression of TUBB5 and SHANK3 gene, equal to 4.077 and 11.345 times respectively. no significant difference was shown in DDC gene experession. Image J sowftware results showed partial microcephaly in treatment group.

Conclusion: The results show that the antidepressant drug of Venlafaxine affects the expression of genes involved in brain development and impairs brain development and mental disorders in the fetus. As a result, the use of this drug by the mother during pregnancy and lactation due to irreparable damage to the fetal brain, including fetal microcephaly and hyperactivity, etc. should be prohibited.

Keywords: Gene Expression, Brain Disorders, Antidepressant, Venlafaxine, Pharmacogenomics

Study The Affections Of Olfactory Stem Cells On The Treatment Of Parkinson's Disease: A Systematic Review (Review)

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Introduction: Parkinson's disease (PD) is one of the neurodegenerative disorders. It is caused by destroying dopamine-secreting cells. PD is an incurable disease but some methods such as surgery, drugs, physiotherapy can suppress or control the disease process. It is noteworthy studies have also suggested stem cell therapy and these days the effect of olfactory stem cells on PD is controversial. This study aims to review the papers about the new treatment.

Methods: We searched on PubMed, Cochrane, science direct, and Google Scholar database from 2012 to February 2020. 76 papers were found. 61 of them were excluded because of their irrelevant abstracts. Finally, we study on 7 papers that all were English.

Results: Results: Based on the studies, the cellular sources used were olfactory ecto-mesenchymal stem cells (OEMSCs), adult human olfactory epithelial-derived progenitors (AHOEPs), and olfactory bulb neural stem cells (OBNSCs). OEMSCs could express dopaminergic neuron markers at mRNA and increased the dopamine transporter and tyrosine hydroxylase. It was a good source of stem cells because of different reasons such as easy harvest and high proliferation. AHOEPstested in animal models. The result showed that about 35% of the animals improved behavioral recovery. During these experiments, no evidence of tumorigenesis was found. Using OBNSCs, increased the percentage of improvement. In other research, it can reduce movement disorders in a rat model of PD. Compared with OBNSCs and OE-MSCs as two sources of olfactory stem cells, the mRNA expression of the dopaminergic activity markers from OB-NSCswas significantly higher than the other one. The superiority of OE-MSCs was noninvasive and easier harvesting process, faster proliferation, and longer life span. Some studies have examined the conditions of treatment with stem cells. For example, a hypoxic environment promotes OEMSCsinto dopaminergic neurons by increasing the expression of hypoxia-inducible factor-1α, activating the tyrosine hydroxylase gene and the level of dopamine cells.

Conclusion: Given the wide diversity of stem cells in the treatment of PD, olfactory stem cells have a better effect on treatment compared to the rest. But more studies are needed to compare the types of olfactory stem cells together.

Keywords: Parkinson's disease, Olfactory, Ecto mesenchymal stem cells, Treatment.

Study the awareness and the role of education on cervical cancer prevention(Systematic Review) (Review)

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Introduction: Cervical cancer (CC) is the fourth leading agent of cancer and the second most common cancer among women. Among the factors that are effective in the occurrence of this agent can be pointed to the lack of developed educational programs and the lack of awareness about CC. Studies show a lack of women's awareness and the lack of proper education and consequently increase this cancer. Therefore, it can be said that educating and raising women's awareness in this field is effective in preventing and reducing CC. Considering the importance of education in the prevention of CC, this study was conducted to investigate the level of women's awareness about CC and the role of education in the prevention of this cancer.

Methods: By researching in PubMed, Google Scholar, and Sid databases from 2015 to 2020 found 96 articles. 32 articles were excluded with checking title, 25 articles were excluded with reading the abstract, and 10 articles were excluded by reading the full text. Finally, 29 articles were selected for review. The language of all articles was English.

Results: The following results were obtained by studying 11 clinical trial articles: Suffering from CC is one of the leading causes of cancer death worldwide. Efforts to raise the level of education and awareness of women to prevent CC through educational intervention is an important step in women's health. Previous articles have shown that when women become aware of the causes and risk factors for cervical cancer, they are probably taking steps to become aware of the prevention of this cancer. Educational interventions have increased women's awareness, knowledge about CC, and its prevention. Women who have received training programs have more knowledge about CC prevention

Conclusion: According to the articles and examining the level of women's awareness about CC and the role of education in the prevention of CC, it can be said that increasing the level of awareness and education is directly related to CC prevention. Due to the greater focus of previous studies on the effect of vaccination on CC prevention, it is recommended that preventive strategies be used in future studies.

Keywords: prevention, Education, women, cervical center

Studying the impact of estradiol on CD90 positive spermatogonial stem cells viability (Research Paper)

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Introduction: Until now, there are controversies about effect of estradiol on regulation of reproductive function and fertility in males. In this study we investigated the possible adverse/positive effects of estradiol on male murine germ cells in-vitro after seven days.

Methods: Following testicle tissue sampling, single- cell suspensions were harvested using 0.25% Trypsin/EDTA solution. CD90 positive cells were enriched using magnetic activated cell sorting technique. CD90 positive cells then were treated with different concentrations of estradiol ranged between 500µg/ml and 0.01ng/ml. After 7 days of treatment, cell survival rate was monitored using conventional MTT assay.

Results: Our findings revealed that, estradiol could potentially increase the viability of CD90 positive cells in a dose dependent meaner compared to the non-treated control cells ($P<0.05$).

Conclusion: These results showed that, estradiol could have positive effect on survival of CD90 positive cells in-vitro in male germ cells.

Keywords: CD90 positive cells; spermatogonial stem cells; Estradiol; Cell vaibility

Sub-types of Stroke Associated with Pregnancy (Review)

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2.

Introduction: Stroke is one of the main agents of mortality in advanced societies. Brain ischemia is a destructive phenomenon for pregnant women; because this phenomenon can lead to death or long-term disability and affect the family as well as the not born child. It is important to note that patterns of stroke affecting pregnant women differ from the non-pregnant female population at childbearing age.

Methods: This review study, conducted in 2020, includes articles were from Pub med, Scopus, Web of Science, and Google Scholar databases. Articles that did not have sufficient information about sub-types of stroke were excluded from the study.

Results: Hemorrhagic strokes and ischemic strokes are the most common types of stroke in pregnant women. Among the ischemic strokes, the highest was arterial occlusions, and then venous occlusions. The most common cause of arterial occlusions was cerebral vasoconstriction syndrome. Major causes of hemorrhage were aneurysm, then arterial-venous malformation, pregnancy-induced hypertension, and HELLP syndrome [hemolysis, the H in the acronym, elevated liver enzymes (EL), and low platelet count (LP)]. Hemorrhagic stroke revealed a much weaker forecast and with less abundance than ischemic stroke. Hyper-coagulable, pre-eclampsia, and thrombo-embolic diseases with elevated pro-thrombotic biomarkers and increased cerebrovascular disease were less frequent than the other two diseases.

Conclusion: There are different types of stroke-related to pregnancy. Ischemic stroke is the most common type of stroke among pregnant women. The existence of cerebrovascular diseases and cerebral vasoconstriction play an important role in Ischemic stroke and hemorrhage stroke.

Keywords: Stroke, Pregnancy, Women

Sumac Nano-phytosome improves oxidative stress in prenatal Valproic acid-induced Rat model of autism (Research Paper)

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Introduction: Autism Spectrum Disorders (ASD) are characterized by social and communication deficits, and by repetitive behavior and restricted interests. Rhus coriaria L. (Anacardiaceae), widely known as sumac plant, is also valued for both its nutritional qualities and medicinal values. It is also commonly used as a medicinal herb in Persia. Phytosomes are drug carriers used to improve vesicular drug delivery systems wherein they are bound and linked with lipoid membranes and phospholipid molecules. Autism Spectrum Disorders (ASD) are characterized by social and communication deficits, and by repetitive behavior and restricted interests. Rhus coriaria L. (Anacardiaceae), widely known as sumac plant, is also valued for both its nutritional qualities and medicinal values. It is also commonly used as a medicinal herb in Persia. Phytosomes are drug carriers used to improve vesicular drug delivery systems wherein they are bound and linked with lipoid membranes and phospholipid molecules. The aim of this study was to investigate the effects of sumac Nano-phytosome on antioxidant enzyme in Valproic acid-exposed rat offspring.

Methods: Offspring male rats were segregated into seven groups; Group-1 served as control, received a single intraperitoneal injection of saline maternally on E12.5. Group-2 received sodium valproate (500 mg/kg in 0.9 % saline, i.p) maternally on E12.5 was considered as VPA-exposed group, Group-3 to 4 were VPA-exposed which received sumac and sumac Nano-phytosome (40 mg/kg/day, PO) for 4 weeks respectively.

Results: Our results showed the prenatal Valproic acid-exposed rat increased level of oxidative stress was found by determining superoxide dismutase(SOD)and catalase activities ($P < 0.001$) and Sumac Nano-phytosome treatment reduced the oxidative stress in brain ($p < 0.01$).

Conclusion: In conclusion, prenatal exposure to Valproic day in pregnant rat leads to the development of autism like features. Sumac Nano-phytosome reduced the oxidative stress in animal model of autism presumably by its antioxidant activity.

Keywords: Sumac Nano-phytosome, Autism, Valproic acid, Oxidative stress

Systemic sodium valproate ameliorates impaired short-term memory due to associative morphine analgesic tolerance (Research Paper)

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Introduction: Repeated morphine without consistent contextual pairing yields non-associative morphine analgesic tolerance; while prolonged or repeated opioid injections in the presence of specific environmental cues can induce tolerance specific to that setting which named associative morphine analgesic tolerance. Namely, ability to learn and memorize could be ruined by morphine exposure. Effects of a tolerance alleviator sodium valproate on memory impairment were therefore examined in morphine tolerant rats.

Methods: To induce associative tolerance, we used male Wistar rats, weighing 250-300 g at the beginning of experiment. Rats received morphine sulfate (4 mg/kg), s.c. in one of two distinct environments and on alternate days, s.c. saline (2 ml/kg), in the other environment for 13 days. To produce non-associative tolerance, morphine sulfate was injected at their home cages for 8 days. Rats were randomly assigned to saline, morphine (associative and non-associative), sodium valproate (250 mg/kg) and sodium valproate+ morphine groups. Sodium valproate was administrated one hour before morphine sulfate treatment daily to investigate the effects of it on tolerance development. Analgesia was assessed during the tolerance developing period using the Hargreaves apparatus. Following tolerance development, short-term memory was tested using a Y-maze task.

Results: After several administrations, morphine was ineffective when given in the environment in which the rat had previously received morphine o day 13. However, the same dose of morphine was fully effective when administered in the context previously paired with saline on day 14. Thus, using this behavioral protocol and method of drug administration, the analgesic tolerance to morphine could be accounted for by learning factors and therefore was associative. Animals were tolerant to morphine in home cages, indicated that the morphine tolerance observed in these animals was largely independent of context (non-associative). Data showed that sodium valproate alone did not show analgesic effects; nevertheless, administration of valproate along with morphine was acted as an adjuvant analgesic to reverse the development of morphine tolerance. Moreover, chronic morphine impaired short-term spatial memory, while sodium valproate did not impair short-term spatial memory on its own, but sodium valproate treatment an hour before each morphine injections did not prevent this impairment in non-

associative morphine analgesic tolerance. Furthermore, no difference was seen in locomotion across the groups.

Conclusion: short-term memory was impaired via both types of morphine tolerance in the Y-maze task. Sodium valproate did not have any analgesic effect and did not impair short term spatial memory on its own, but administering sodium valproate one hour before each morphine injections can improve short-term memory impairment in associative morphine analgesic tolerant rats.

Keywords: Associative morphine tolerance, Opioid, Valproate sodium, Short-term memory

Targeted magnetite nanoparticles as a drug carrier and thermal sensitizer agent in glioblastoma cancer cells (Research Paper)

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Introduction: Hyperthermia is a promising adjuvant therapy for cancer treatment. Localized hyperthermia is one of the most challenging problems in chemo-hyperthermia therapy. In the present study, magnetite nanoparticles as a carrier of chemotherapy drug modified with folic acid-ligand (TMZ-MNP-FA) were designed for targeted chemotherapy and a thermal-sensitizer agent for alternating magnetic field (AMF) hyperthermia of cancer cells.

Methods: Nanoparticles were characterized and in vitro AMF-triggered release of them using diffusion method were evaluated. The magnetic properties of the nanoparticles were evaluated by a vibrating-sample magnetometer and the specific absorption rate (SAR) of the nanoparticles was determined. The C6 glioblastoma cancer cells were treated with the nanoparticles and subjected to an alternating magnetic field to reach a typical hyperthermia temperature of 43 °C. The cytotoxic effects of various treatments were assessed using Annexin V-FITC/PI assay.

Results: The in vitro release studies exhibited that the drug release from TMZ-MNP-FA nanoparticles was minimal at 37 °C but was noticeably boosted under an AMF irradiation. The SAR value of TMZ-MNP-FA NPs was 530 W/g indicating that these nanoparticles could serve as a powerfull thermal sensitizer agent under an AMF irradiation. Our results showed that combined magnetite chemo-hyperthermia (AMF+TMZ-MNP-FA) treatment was significantly more efficacious in cancer cells than hyperthermia, chemotherapy, or chemo-hyperthermia treatments ($P < 0.0001$).

Conclusion: In conclusion, TMZ-MNP-FA had a key role to convert the externally delivered radiofrequency energy to heat in cancer cells. Moreover, localized combined chemo-hyperthermia with TMZ-MNP-FA under an AMF was a more effective approach to kill cancer cells

Keywords: Glioblastoma cancer, Alternating magnetic field, Localized hyperthermia, Targeted nanoparticle

Targeting apoptosis Pathways on Malignant Human Glioma Cell Line by Cytochalasin H (Research Paper)

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Introduction: Glioblastoma is one of the most malignant central nervous system tumors located in the brain . This is characterized by the code 3/9440 in the International Classification of Diseases for Oncology. Despite the efforts carried out to improve the glioma tumor's treatment, these tumors are not curable. Although chemotherapy is effective in the tumor treatment but the drugs used in the treatment have side effects for the patients and sometimes, drug resistance causes limitations in the treatment of the patients. Therefore, the investigation of new therapeutic approaches for this disease is very important. we are needed to explore molecular mechanism for treatment. Cytochalasins connect to their sub-units, leading to some alterations in the cytoskeleton structure and preventing polymerization. Thus, formation of microfilaments is significantly inhibited .Moreover, cytochalasins prevent cell transfer and create enucleated cells by penetrating the cell membrane. Apoptosis is the consequence of a planned intracellular cascade of genetically controlled stages. On this basis, the aim of current study was to provide a proof-of-concept on the mechanism of caspases-activities in the apoptotic pathway after treatment of malignant human glioma cell line (U87MG) by cytochalasin H and stud ied the morphology of the cells treated with cytochalasin H by inverted microscope and Fluorescence Microscope.

Methods: we examined the cytochalasin H cytotoxicity activities as a new agent therapeutic on the human malignant glioma cell line (U87MG) in vitro. The cells were cultured and treated with 10 -5 - 10-9 M of cytochalasin H for 24, 48 and 72 h. MTT assay was used to assess Cytochalasin H cytotoxic effect on human malignant glioma cell line (U87MG). Different concentrations of cytochalasin H (10-5 and 10-9 M) for 24, 48 and 72 h and each concentration has 8 replicate wells. Fluorometric of caspase 3, 8, and 9 activities were carried out using the caspase assay kit (Novex)and Morphology changes in the U87MG cells were examined by fluorescence microscope.

Results: MTT assay showed that cytochalasin H at concentrations of 10-5 M inhibited the U87MG cancer cells proliferation for 48 h ($p<0.05$). but there was no cytochalasin H toxic effects on the cell line U87MG for 24 and 72 h ($p>0.05$) and as well as was not observed cytochalasin H toxicity effects on normal cell line HEK Compared with the U87MG cancer cells ($p>0.05$). After treatment U87MG with 10-5 M CH for 48 h, Using a caspase assay kit (Novex). Activity of caspase-3, caspase-8 and caspase-9 were increased following CH treatment (17% , 12% and 7% respectively) but this was not a significant difference ($p > 0.05$). The structural changes of the cells treated with CH compared with the control was investigated.Moreover ,the fluorescence microscopy indicated morphological changes due to apoptosis in U87MG cancer cells after treatment with cytochalasin H. The results obtained from this study show that the enzyme activity of the caspases is not sufficient to start the caspase-dependent apoptosis process. These

results were inconsistent with the findings obtained from testing the cells by fluorescent microscope. The cell nuclei were observed, condensed, and fragmented under fluorescent microscope, and this is how the cells were led towards apoptosis. So, the effect of cytochalasin H on the induction of apoptosis in the U87MG cells could probably be attributed to the caspase-independent apoptosis pathway.

Conclusion: This study shows the effect of caspase-independent pathways of the programmed cell death on the U87MG cancer cell line under cytochalasin H treatment. Further studies are needed to explore the another mechanism.

Keywords: Caspases, Cytochalasin H, Glioblastoma, apoptosis

TargetingTherapy with Recombinant Drugs Against Angiogenesis in Cancer (Review)

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Introduction: Angiogenesis is a physiological pathway by which new blood vessels form the existing vessels. Solid tumors require blood if they grow to more than a few millimeters in size. These new vessels are triggered by various stimuli such as hypoxia, vascular injury or angiogenesis growth factors that act as environmental stimuli. This process must be controlled under harsh conditions, and loss of balance may cause pathological distress such as tumorigenesis. Tumor angiogenesis is one of the main features of cancer cells, whereby new blood vessels are formed adjacent to the tumor. New blood vessels thus supply "growing tumors" with oxygen and nutrients; And cancer cells invade surrounding tissue, move throughout the body. Therefore, rearrangement of angiogenesis factors stimulates tumor growth and metastasis. These angiogenic properties have strengthened the anti-angiogenic therapeutic target with recombinant drugs.

Methods: In this review article, the keywords "therapeutic targeting" AND"recombinant drugs" OR "cancer" AND "angiogenesis". Search PubMed, ScienceDirect and Google Scholar databases

Results: Due to the importance of the angiogenic process in cancer, in this article, the achievements and factors related to the targeting therapy against angiogenesis and the future perspective of cancer therapy by anti angiogenesis agents was reviewed

Conclusion: Angiogenesis targeting is more effective in cancer treatment. In addition the use and sale of these recombinant drugs has increased in recent years, this is a one reason for the success of recombinant drugs.

Keywords: TargetingTherapy‹Recombinant Drugs ‹Cancer ‹Angiogenesis

The antibacterial effect of zinc oxide nanoparticles were synthesized by co-precipitation and wet chemical methods on Escherichia coli bacteria (Research Paper)

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Introduction: Nanoparticles are particles with dimensions less than 100nm that due to their very small size and surface to volume ratio, have high properties and performance, including antibacterial properties. So far, the antibacterial properties of nanoparticles have been investigated on a variety of bacteria. Nanoparticles are produced in different ways such as co-precipitation, chemical wet with inhibitor, microwave, and ... In this paper, the antibacterial power of ZnO nanoparticles that has been investigated by both sediment and chemical methods wet with inhibitor.

Methods: Materials required for the co-precipitation method: ZnCl 1.36 gr, NaOH 1.6 gr, and distilled water. Production of ZnO nanoparticles by co-precipitation method At first, combine 1.36 g of ZnCl and 1.6 g of NaOH in separate beakers in distilled water and bring each to a volume of 100 cc. Next, place two beakers on a heater and a magnet and by placing a few magnets in beakers, we turn on the devices and wait until the material reaches the boiling point. Then, we add the contents of two beakers to each other. As soon as the contents of the beakers are mixed, the white substance ZnO is produced. The nanoparticles are washed several times and then sterilized by using UV light. Afterwards, we determine the concentration of nanoparticles. To determine the concentration, we put 5cc of the produced material in a plate and weigh it. By placing the plate in the oven, drying it completely and weigh it again. In this case, we have the amount of grams in 5cc and it is possible to calculate the concentration in grams per liter with simple calculations. Using the UV spectrophotometer, we read the maximum wavelength of its UV absorption and measure the optical size of the produced nanoparticles by performing mathematical calculations. The size of nanoparticles produced by this method was reported to be 5-6nm. After producing nanoparticles, we create 6 wells in the culture medium of Ecoli bacteria and in the wells, nanoparticles added with the concentrations of 14gr / lit, 7gr / lit, 3.5gr / lit, 1.75gr / lit, 0.87gr / lit and additional control, respectively. Place the plates in the incubator for 24 hours and check for inhibition zone conditions. Production of nanoparticles by wet chemical method with inhibitor Weigh the ingredients as before and dissolve them in distilled water to a volume of 100cc. Pour ZnCl into a balloon and place it on th heater and magnetic stirrer. Attach the soxhlet to the balloon and pour mercaptoethanol inhibitor into it. Add a drop of mercaptoethanol every 3 seconds. When the mercaptoethanol is finished, fill the inside of the soxhlet with NaOH and allow it to be added to the material at the same rate. Gradually, white ZnO nanoparticles are produced in the balloon. Sterilize the resulting material as a co-precipitation method and determine the concentration and finally calculate its optical size. The size of nanoparticles is 4-5nm. By creating 6 wells in the plate, ZnO nanoparticles which produced by chemically wet with inhibitor with concentrations of 2gr / lit, 1gr / lit, 0.5gr / lit, 0.25gr / lit, 0.125gr / lit, and 2gr / sample are poured without washing,

respectively and after 24 hours of incubation, check the plates for diameter in a state of non-growth halo.

Results: In this study, zinc oxide nanoparticles were produced by co-precipitation and wet chemical methods with optical sizes of 5 and 4 nm, respectively. Then, to investigate its antibacterial properties, it was done by plate drilling and grass culture with concentrations of 10, 2.5, 1.25, and 0.62 for co-sedimentation method and concentrations of 2, 1, 0.5, 0.25, and 0.125 g / l for wet chemicals. In addition, in the wet chemical method, because it was synthesized with mercaptoethanol inhibitor, it was used in a well without washing nanoparticles with a concentration of 2 g / l. The results showed that zinc oxide nanoparticles synthesized by wet chemical method have inhibitory properties on bacterial growth. Also, the diameter of the growth inhibition halo decreases with decreasing concentration, and the maximum halo is related to the concentration of 2 g / l with a size of 13 mm and unwashed nanoparticles of 16 mm. The reason for the difference is the inhibitory effect.

Conclusion: According to the observed results, ZnO nanoparticles produced by co-precipitation method with an optical size of 5-6nm in none of the concentrations have not shown in non-growth halo in Ecoli bacterial culture medium. And it seems that the nanoparticles produced in this way have not been able to develop antibacterial properties against Ecoli bacteria. However, in the use of ZnO produced by wet chemical method with inhibitor with optical size of 4-5nm, despite the use of much lower concentration, at a concentration of 2gr / lit, a state with a diameter of 13 mm has been observed. And if the nanoparticles are not washed with the same concentration, a non-growth halo with a diameter of 16 mm is created. It can be concluded that the use of different methods of nanoparticle production due to the creation of different optical sizes and other properties in nanoparticles also create different properties. For example, nanoparticles produced by wet chemical method have more antibacterial properties than co-precipitation method.

Keywords: Nanoparticles Zinc oxide Wet chemical Co-precipitation E coli

The antibacterial effects of iron oxide nanoparticles on Pseudomonas aeruginosa (Research Paper)

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4.

Introduction: Pseudomonas aeruginosa is an opportunistic pathogen resistant to many antibiotics and disinfectants that causes severe acute and chronic nosocomial infections in immunocompromised, catheterized, or burn patients. The new attributes of materials in nanoscale have made nanotechnology one of the leading sectors in all sciences including biology and medicine. In this regard, iron-based magnetic nanoparticles owing to their low toxicity and various capabilities, have been noticed by researchers. Increasing resistance to common antimicrobial agents is one of the major problems in healthcare today. Controlling the prevalence of bacteria in different environments is an important challenge in these parts that overcoming them is very significant from a health and economic. Identification new antibacterial effectors is necessary to overcoming resistant strains. The aim of this study was to investigate the effect of iron oxide nanoparticles in inhibiting the growth of Pseudomonas aeruginosa.

Methods: In this experimental and laboratory study, the antibacterial effect of iron oxide nanoparticles on Pseudomonas aeruginosa was determined by MIC (Minimum Inhibitory Concentration) and MBC (Minimum Bactericidal Concentration), disk diffusion and well method in Muller Hinton broth and agar.

Results: In this study, a concentration of 5 mg/ml iron oxide nanoparticles did not have a significant effect on bacteria, while concentrations of 10mg/ml and 20mg/ml causes a considerable decrease in the number of bacteria in the treatment group compared to the control group.

Conclusion: Iron oxide nanoparticles have a significant effect on Pseudomonas aeruginosa. According to the obtained results and the inhibitory and bactericidal effect of iron oxide nanoparticles, these nanoparticles can be used in pharmacy and treatment of nosocomial infections, as well as the production of new disinfectants.

Keywords: Iron oxide nanoparticles, Pseudomonas aeruginosa, Antibacterial effects, MIC and MBC, Disk diffusion

the application of fermentation in production of pharmaceutical drugs (Review)

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1.

Introduction: Introduction and generalities The term biotechnology was first used by Karl Erkey in 1919; The use of the term means to convert raw materials into a specific product using living organisms, as well as to introduce the concept of genetic modification. (Almedia et al.٫٢٠١٣) Since then, the applications of biotechnology have gained a broader meaning, and it became this way by using living organisms to produce products for human consumption or to solve human problems (Theian and Palladino, 2014). Biotechnology is based on a body of knowledge from various sciences including: microbiology, biochemistry, genetics, engineering and computer sciences, etc. In recent years, due to the benefits of this science, the advances in the biotechnology industry have been very significant, such as: the production of high efficiency products, products which require low or minimal man power, products which have a low cost of production and finally but not limited to the environmental friendliness of this industry and it's reduction of greenhouse gas emissions. In the pharmaceutical industry, efforts to discover new drugs using biotechnology industry have grown tremendously and with that being said The largest pharmaceutical companies in the world Are in someway related to biotechnology research and production by this method (Almedia et al.,2013). One of the processes in this industry that is considered to produce various compounds, especially medicinal compounds, is the fermentation process. The word fermentation is derived from the Latin verb fervere meaning to boil, and actually refers to the formation of carbon dioxide bubbles in the process. (Stanburyet al.,2017) Fermentation occurs naturally in many foods and since ancient times humans (peoples of the Indian subcontinent, Egyptians, Chinese, Greeks) have used this process to produce some products such as bread, yogurt, cheese and also various Beverages. (Kuila and Sharma,2018). Today, the term fermentation has a broader meaning and means the deliberate use of microorganisms such as bacteria, yeasts and fungi to produce products useful to humans. (figure 1). (Paulov Paul and Branyik 2013) Since the introduction of genetic engineering on a practical scale in the 1970s, there has been a great deal of interest in producing biological products using fermentation and in saying this Many researchers have tried to study new sources produced by microorganisms. (Sitanggang et.al.,2010)

Methods: In this article, we reviewed and collected valid articles from specific sites and gernals and after reading all of them, we prepared a summary of their valuable data and in the form of tables and even shapes with their full description in the article.

Results: The success of the food fermentation process depends on the action of microorganisms, the growth and activity of microorganisms, And all of these conditions in turn depend on environmental conditions, And therefore by controlling environmental conditions we can stimulate the growth of a microbial species, And fianally By forgoing these changes we then in turn are resulted with a large number

of desired products. In the Khalilzade high cell density culture method, the highest cell density is obtained using the batch feed culture fermentation process (HCDC) (2004, et.al.) The many advantages of the SSF method include the production of primary metabolites, some including low energy requirements, low consumption, low waste and easy product recovery without the need for a sterile environment. For a successful extraction using the SSF process it is necessary to have fermentation parameters such as humidity, temperature, pH, Aeration and Oxygen Transfer, Cylinder Size, Growth Estimation, and Growth Characteristics present in order for the process to go smoothly (Saykhedkar and Singhal 2004).

Conclusion: Due to the magnificent process of fermentation The progress of this science is increasing day by day leading to a large number of biotechnology companies researching innovative methods for producing effective drugs to save more people's lives and that's why we are here to add value to others and improve our quality of life.

Keywords: fermentation-drugs-biotechnology-genetic-human

The Association Between Dietary Zinc Intake and Health Status,Including Mental Health and Sleep Quality, Among IranianFemale Students (Research Paper)

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Introduction: Epidemiological studies have suggested that there is an association between diet and mental health. The aim of the current study was to explore the association between dietary zinc intake and risk of depression, anxiety, and sleep quality distortion among female students of the Semnan University of Medical Sciences in a cross-sectional study.

Methods: From January through October 2019,142 female students were randomly selected from the Department of Nutrition and Food Science at the Semnan University of Medical Sciences by simple random sampling. Food frequency questionnaires (FFQs) were used to assess participants' dietary intake over the past 12 months. Depression, anxiety, and sleep quality were examined by the Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), and Pittsburgh Sleep Quality Index (PSQI), respectively. In the analysis, the crude model was adjusted for total energy intake (kcal), while the model was adjusted for energy intake (kcal), age, economic status, physical activity level, serum vitamin D level, and body mass index.

Results: Dietary zinc intake is significantly associated with depression (odds ratio (OR) (95% confidence interval (CI)): 2.34 (0.38–4.30)) and anxiety (OR (95% CI): 3.43 (2.36–4.50)), sleep disorders (OR(95% CI): 3.65 (2.16–5.13)), sleep duration (OR (95% CI): 2.62 (0.39–4.86)), and daytime dysfunction (OR (95% CI): 5.31(2.84–7.78)) in the model, as well as sleep delay (OR (95% CI): 1.80 (1.05–2.55)) and mental quality of sleep (OR (95% CI): 1.63(1.10–2.15)) in the crude analysis.

Conclusion: This cross-sectional study supports the inverse association between dietary zinc intake and mood disorders, including depression and anxiety, and some indices of sleep disturbance in the Iranian female students. Further cohort or

intervention studies are required to draw a firm link between dietary zinc intake and mental health

Keywords: Dietary zinc.Depression.Anxiety.Sleep quality.Students

The Association between Maternal Dietary Iron Intake during the First Trimester of Pregnancy with Pregnancy Outcomes and Pregnancy-Related Complications (Research Paper)

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Introduction: In this study, we investigated the associations of maternal dietary iron intake during the first trimester of pregnancy and pregnancy outcomes and related complications in pregnant women of Isfahan, Iran.

Methods: In this prospective study, 812 healthy first-trimester singleton pregnant women were selected randomly from 20 various health centers across Isfahan city during 2015–2016. The maternal dietary iron classified into 2 groups, including heme and non-heme iron. Factors including pre-eclampsia, gestational hypertension, gestational diabetes mellitus, intrauterine growth restriction (IUGR), and nausea and vomiting in pregnancy considered as the pregnancy-related complications. Infant's birth weight, birth height, and birth head circumference were also determined as the pregnancy-outcomes.

Results: There was a significant association between total iron consumption and infant head circumference ($p = 0.01$). Total maternal iron (the sum of heme and non-heme iron) was negatively associated with both infant's birth height ($p = 0.006$) and birth weight ($p = 0.02$). Non-heme iron consumption is positively associated with high-risk of IUGR ($p = 0.004$). Heme intake was associated with an increased risk of maternal fasting blood sugar (FBS) ($p = 0.04$). Higher heme, non-heme, and total iron intake were associated with lower risk of pre-eclampsia (heme: crude $p = 0.05$; non-heme iron: adjusted $p = 0.02$; total iron: adjusted $p = 0.05$).

Conclusion: Maternal total iron intake was directly associated with infant head circumference, whereas, negatively associated with both birth weight and birth height. High non-heme iron intake may increase the risk of IUGR, and a high intake of heme iron may increase FBS.

Keywords: Dietary iron; Pregnancy outcome; Heme

The association between obesity and severe COVID-19: A systematic review (Review)

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Introduction: Coronavirus disease 2019 (COVID-19) is a novel threat that seems to result from the collusion between a new pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and an existing pandemic of metabolic disease driven by obesity. Obesity, a silent killer which is increasingly prevalent globally and patients with obesity are at increased risk of exacerbations from viral respiratory infections. This study is to determine the association between obesity and severe COVID-19.

Methods: In this study all papers from 2016-2020 were identified in a search of Elsevier, PubMed and SID, Google Scholar databases. Finally 70 studies that the association between obesity and severe COVID-19.

Results: The findings of this systematic review suggested that Obesity (BMI≥35 kg/m2) was recently identified as a major risk factor for worse COVID-19 severity and the need of intensive care, especially among the young (patients aged <60 years). Patients with obesity with COVID-19 are 7 times more likely to need invasive mechanical ventilation than are patients without obesity. Obesity is closely linked to DM, hypertension and cardiovascular disease, aforementioned risk factors for severe COVID-19. Physical inactivity, common in obesity, may lead to impaired immune response. The altered dynamics of pulmonary ventilation with reduced diaphragmatic excursion and a relative increase in anatomical dead space may account for the increased incidence of severe COVID-19 in patients with obesity. Adipose tissue is also a source of many pro-inflammatory mediators and adipokines such as C-Reactive protein, interleukin 6, hyperleptinemia with Leptin resistance, hypoadiponectinemia and high serum concentrations of TNF-α and IL-17A associated with obesity explains the preexisting inflammatory state in obese individuals which predisposes them to worse outcomes and fatality. Increased adipose tissue and lowe Vitamin D serum levels in obesity could lead to increased ACE-2expression (which is the putative co-receptor for cellular SARSCoV-2 entry) and risk of infection.

Conclusion: The study finding shows obese patients especially in younger patients aged had increased odds of progressing to severe COVID-19. As the severe acute respiratory syndrome coronavirus 2 may continue to spread worldwide, clinicians should pay close attention to obese patients, who should be carefully managed with prompt and aggressive treatment

Keywords: obesity, COVID-19, respiratory physiology, immunity

The Bioinformatics Analysis of Direct and Indirect Role of Diet by Affecting the Microbiota of Colon in Colorectal Cancer Development (Research Paper)

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Introduction: Colorectal cancer (CRC) inflammation, regardless of its cause, if turned into chronic, especially during the late stages of cancer, can help the progress of CRC. Inflammation in the colorectal part of the body can be affected by microbiota, as well as an individual's diet. Evidence is showing a relationship between specific diets, inflammation, and CRC. It could be concluded that a change in diet could affect microbiota in intestines as well as their metabolites. This study aims to analyze microbiota and diet-related inflammations, causing mechanisms that support tumors in patients.

Methods: The GEO database has been used to select and analyze of Microarray dataset. Three GSE number has been chosen, and Venny diagram highlighted common differential gene expressed (DEG). The functional annotation analysis of selected DEGs manifests the multiple roles of diet in CRC and colon microbiota.

Results: The results show, the dysbiosis caused by Inflammatory and low fiber food products, occupies immune cells with invasive bacteria that have had the chance to grow, leading to inflammation and the severity of these parts cancerous cells. Additionally, considering the critical role of vegetable oils and unsaturated fatty acids in reducing CRC risk compared with animal fat and the positive effect of these oils on the expression of a group of genes related to inflammation and colon cancer to reduce the risk of CRC was investigated by bioinformatics analysis.

Conclusion: Inflammation plays a crucial role in malignant CRC and can make it worse. Inflammation could be a result of diet can play a role by affecting the microbiota and worsen the inflammation. Other than the indirect effect of diet through inflammation on CRC, the direct impact of some nutrition that contains carcinogens could also affect this disease.

Keywords: Inflammation, Colorectal Cancer, Microbiota, Diet

The Comparison between Polynomial Regression, Generalized Additive Models and Functional Regression for Sparse data, the Children Height and Weight case study. (Research Paper)

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Introduction: Functional Data analysis is a branch in statistics that considers the underlying curves for the observed data with dimension reduction methods. The observations are recorded dense or sparse over the domain. In this research, we compare polynomial regression, generalized additive models, and functional regression for sparse data in the children's height and weight dataset.

Methods: The weight and height data are not recorded for every child in every time points, therefore there are some missing values within curves. The standard statistical models have some limitations and they do not capture the behavior of the curves. We find the optimum bandwidth for polynomial regression and generalized additive models by grid search. In this regard, we randomly split the dataset for training and testing the models and we compare them with mean square prediction error. We also register, align, approximate, and smoothing the curves by B-Spline basis functions and generalized cross-validation, respectively.

Results: The outliers were removed and the underlying curves for the height and weight of children were estimated with the optimal bandwidth and generalized cross-validation, respectively. They have an increasing pattern.

Conclusion: The sparse functional data are common in the different disciplines and we compare three statistical methods for modeling them. The polynomial regression, splines in the generalized additive models, and B-Splines as basis functions for functional regression models. We conclude that the behavior of the estimates is not very different from which other.

Keywords: Height, Weight, Children, Sparse Data

The correlation between IL-6 and IL-10 expression in symptomatic children with HHV-6 infection (Research Paper)

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Introduction: Human Herpes Virus-6 is a cause of common childhood exanthemas with symptoms such as high fever and skin rashes. Given the clinical manifestations of the virus disease, the immune responses especially the correlation between the expressive inflammatory (i.e. IL-6) and anti-inflammatory (i.e. IL-10) cytokines may play a key role in the immunopathogenesis of the disease. We designed this study to investigate the correlation between IL-6 and IL-10 in symptomatic children with HHV-6 infection.

Methods: For the present study, we randomly used 25 PCR-confirmed throat specimens for HHV-6 collected from children aged <5 years old with at least fever and rash as two main clinical pictures. Real-time PCR was performed on all these 25 specimens using specific primers. Finally, the results were analyzed by PRISM 2008 software.

Results: Despite the absence of the same study, we found a positive significant correlation between the expression of IL-6 and IL-10 in HHV-6-infected children in the symptomatic phase of illness (P-value: <0.05).

Conclusion: Our study indicated that cytokines and their relationship can implicate in the pathogenesis of acute HHV-6 infection in the early stages of life.

Keywords: Correlation, IL-6, IL-10, Children, HHV-6

The effect digital branding in success and growth of medical centers.
(Research Paper)

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Introduction: Digital branding is a technique that leverages the power of the Internet and digital mediums to develop a brand. Digital branding is a term that's used rather loosely to describe all the different ways in which a business draws in its customers online. It includes a number of different aspects of marketing including SEO, online advertising, content marketing, social media, and influencer marketing. As a business, establishing a brand is key. In the era of online communications, it is just common sense that you must communicate your brand online to stay ahead of the competition. Instead of focusing on one particular product, digital branding highlights more the underlying values of the company. Therefore, digital branding is a more long-term marketing strategy.

Methods: In medical centers ،digital branding means communicating with patients in the right place and at the right time. Digital branding takes traditional brand management principles and applies them to patients' experiences across multiple digital mediums. Many patients research before going to a medical center, which means that if the doctor is not found online, he will lose many new patients. People care less about medical centers that are not found online. Digital branding follows a multi-channel approach to improve your business presence across all channels where your customers are present.

Results: At digital branding strategy, successful medical centers will leverage social media, website content and mobile applications to expand their brand awareness, interact with customers and drive market reach. Today, brands do not need intermediaries in order to have a direct interaction with customers. Digital branding is the deliberate process of creating consistently positive, appealing brand images and messages.

Conclusion: At digital branding strategy, successful medical centers will leverage social media, website content and mobile applications to expand their brand awareness, interact with customers and drive market reach. Today, brands do not need intermediaries in order to have a direct interaction with customers. Digital branding is the deliberate process of creating consistently positive, appealing brand images and messages.

Keywords: Digital branding ،Branding ،Medical centers ،patient ،doctor

The effect of adipose-derived mesenchymal stem cells on renal function and histopathology in a rat model of ischemia-reperfusion induced acute kidney injury (Research Paper)

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Introduction: It has been shown that adipose-derived mesenchymal stem cells (AD-MSC) have protective effects in acute kidney injury (AKI). This study was conducted to assess the therapeutic effects of AD-MSC in rats subjected to acute kidney injury by 45 min of renal ischemia followed by 48 hr of reperfusion (I/R).

Methods: 28 male Wistar rats were divided into four groups, including control, 48-hr sham, 48-hr I/R, and 48-hr I/R receiving AD-MSC. After 48 hr of reperfusion, blood samples were taken from rats' hearts, and 24-hr urines were collected using a metabolic cage. Serum creatinine level (Cr), blood urea nitrogen (BUN), creatinine clearance (Ccr), absolute sodium excretion (UNaV°), fractional sodium excretion (FENa), absolute potassium excretion (UKV°), factional potassium excretion (FEK), and urine osmolarity were measured. Malondialdehyde (MDA) and ferric reducing antioxidant power (FRAP) levels were measured in the right kidney, while the left kidney was used for histologic study after Hematoxylin-Eosin staining.

Results: Renal I/R significantly increased serum Cr, BUN, UNaV°, FENa, FEK, and tissue MDA, and significantly decreased Ccr and urine osmolarity as compared with the sham group. Moreover, histologic studies showed that I/R increased Bowman capsule area, tubular necrosis, vascular congestion, and caused formation of intratubular casts. Administration of AD-MSC at the time of I/R completely or partially protected kidneys from these I/R induced injuries.

Conclusion: Our results show that injection of AD-MSC can reduce degree of renal injury caused by 45 min of ischemia followed by 48 hr of reperfusion in rats.

Keywords: Acute kidney injury Adipose tissue Ischemia-reperfusion injury Mesenchymal stem cells Rats

The effect of aerobic exercise and ginseng on sexual hormones in obese rats (Research Paper)

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Introduction: Infertility and its individual and social problems are one of the most important issues for young couples. About half of all infertility is in men. Aerobic and sexual activity have the potential to improve spermatogenesis and reduce the side effects of obesity. Therefore, in this study, the combined effect of sexing supplementation with aerobic exercise on the fertility of obese mice was investigated.

Methods: In this study, 32 male Wistar mice weighing about 200 to 250 g and average age of 8 weeks were divided into 4 groups of eight. The high-fat diet (45% of calories in fat) was used to induce obesity in mice. The mice trained for five days (1 hour) every week for eight weeks. Simultaneously with exercise, gensing extract was given to the target groups by gavage. After the last exercise session, the animals were anesthetized and their blood was immediately poured into a tube containing EDTA. Also, after measuring body weight, testicles and prostate, samples were taken from the fetuses and some sperm parameters were examined.

Results: The results showed that the weight changes of mice as well as sperm concentration, percentage of normal sperm shape, percentage of motile sperm, adult sperm percentage of rats in all three experimental groups including training group, gensing group and gensing group with difference training It is significant compared to the control group ($P < 0.001$). On the other hand, the results of weight change showed that in none of the studied groups, testicular and prostate weight was not significantly different from the control group ($p < 0.05$). Examination of the results of testosterone changes showed that there was a significant increase compared to the control group in both sexing and sexing groups with exercise ($P < 0.001$). This increase was not significantly different in the exercise group and the control group. The results of counting testicular tissue cell lines showed that there was no significant difference between the groups in any of the spermatogonia, spermatocytes and Leydig and Sertoli cell lines ($p < 05$). Significant differences were observed only in spermatogonia cells in the gensing group with exercise and Leydig cells in the gensing group ($P < 0.05$). The results of testicular spermatogenesis indices showed no significant difference between the groups in any of the TDI, SI and RI indices ($p < 05$). Significant differences were observed only in TDI index in the gensing group with exercise and RI index in the gensing group ($P < 0.05$).

Conclusion: The results of this study showed that aerobic exercise and gensing consumption in both groups improves spermatogenesis indices in the studied groups. In the group of both training and consumption of gensing extract, the improvement of these indicators has been more effective.

Keywords: Infertility, Aerobic exercise, Gensing, Obesity

The Effect of Bone Marrow Derived Mesenchymal Stem Cells on the Survival of Random Skin Flap on Sterptozotocin-Induced Diabetic Rats (Research Paper)

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Introduction: Background & Objective: Wound dressing and healing in diabetic patients is encountered with many problems. This study aimed to investigate the effect of bone marrow derived mesenchymal stem cells (BM-MSCs) on the survival of random skin flap (RSF) on Streptozotocin-induced diabetic rats (STZ) using an optical microscope.

Methods: In this study, 60 male Albino Wistar rats were used (average weight 250-300 gr). The rats were divided into six groups: 1) Health-Non (HN), 2) Health-Cells (HC), 3) Health-Sham (HS), 4) Diabetic-Non (DN) that were became diabetic by injecting STZ 70 mg/kg intraperitoneally), 5) Diabetic-Sham (DS), and 6) Diabetic-Cell (DC). In all groups, the day of surgery was considered as the zero day, on the back area of animal, the flap was created with a size of 8 × 3 cm and the BM-MSCs were performed. The sampling was performed on day 7 after surgery from the region where Transitional Zone (TZ) necrosis was initiated.

Results: BM-MSCs increased the number of blood vessels (P=0.009) and the histology parameters (wound demarcation P=0.0001, granulation tissue P=0.0001) significantly compared to the control group. But this increase was not significant in the area of the survival region.

Conclusion: It was concluded that after treatment with BM-MSCs, the wound healing process in both non-diabetic and diabetic groups was increased in accordance with histological characteristics.

Keywords: Diabetes mellitus, Random skin flap, Bone marrow, Stem cells,Streptozotocin, Survival

The effect of calcitriol on the differentiation of dental pulp stem cells
(Research Paper)

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Introduction: Tissue engineering and regenerative therapies are in progress in the treatment of dental problems, especially endodontics tratments. Induction of mineralization in dental pulp stem cells is of special importance. The aim of this study was to evaluate the effect of calcitriol on differentiation of DPSCs by alkaline phosphatase gene expression and activation assessment.

Methods: In this study was assessed the toxicity levels of different concentrations of calcitriol in 1, 2, 3 and 7 days by MTT assay. Alkaline phosphatase gene expression was determinded by Real Time-PCR and a specific kit was used to determine the alkaline phosphatase activity. Statistical analyses were performed using SPSS software version 17. Statistical significance was determined using t-test and ANOVA.

Results: The results of the present study showed that calcitriol had no toxic effect on dental pulp cells at most concentrations and test times. Also, gene expression and alkaline phosphatase activity in cells treated calcitriol for 7 days showed a significant increase compared to the control group ($p < 0.05$).

Conclusion: Considering the positive effects of calcitriol on dental pulp stem cell differentiation and induction of alkaline phosphatase, these substances can be an intervention modality in bone and dental tissue engineering.

Keywords: Dental pulp stem cell, Mineralization, Alkaline phosphatase, Calcitriol

The effect of climate change and meteorological factors on flowering phenology and pollen season indicators of allergenic plant taxa (Review)

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Introduction: Pollen respiratory allergies have been increasing in prevalence over the last two decades, partly as the result of the impact of climate change. For many allergenic trees, grass and weed species, increased pollen production and prolonged pollination period result in long-term increased abundance of pollen allergens in the atmosphere; earlier shifts of airborne pollen grains and prolonged exposure to respiratory allergens with important health effects on allergic individuals. The aim of this review paper was to investigate the impact of climate change and meteorological factors on flowering phenology and pollen season indicators, with a special focus on the main allergenic taxa worldwide.

Methods: In this paper, we conducted a scientific databases search using nearly 150 related scientific terms and keywords and summarized more than 100 scientific articles related to pollen season indicators, meteorological parameters and climate change. Main variables influencing flowering phenology such as location, climatic and meteorological parameters were identified, discussed and substantiated by published literature

Results: Temperature, solar radiation, humidity, rainfall, wind speed and direction were identified among the most important meteorological parameters affecting the fluctuations of annual concentrations of allergenic airborne pollen grains. Although notable variations were observed according to allergenic species and studied geographical areas, temperature appeared to be the most important climatic parameter affecting flowering phenology and pollen season indicators, especially in tree species. Rising carbon dioxide levels also result in increased plant biomass, increased flowering intensity and pollen production in several tree, grass and weed allergenic species.

Conclusion: There is also a growing body of scientific evidence supporting the fact that carbon dioxide from human activities results in increased plant biomass, increased flowering intensity, and pollen production by stimulating photosynthesis and plant growth and through its influence on the average temperature of the Earth's surface. The present review provides a global picture of the effects of climate change and meteorological factors on flowering phenology and pollen season indicators of allergenic plant taxa worldwide, paving the way for

comprehensive studies in this area of major environmental and public health importance.

Keywords: aerobiology; allergy; airborne; anemophilous; climate change

The effect of conditioned medium derived from endometrial stem cells on expression of stemness genes in endometriosis women (Research Paper)

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Introduction: Endometriosis described as the presence of endometrial tissues outside the uterine cavity. The etiology of endometriosis is unclear, however, probably retrograde menstruation blood cause this disease. It is supposed that menstrual blood-derived mesenchymal stem cells (MenSCs) in endometriosis patients are different from that of healthy women and so, they are responsible for the creation of the disease. Stemness related genes are upregulated in MenSCs of endometriosis patients, so, it was hypothesized that the conditioned medium of these cells from healthy women can affect the expression of stemness genes. The aim of this study was to evaluate the expression of three genes related to the stemness of endometrial stem cells in endometriosis patients in the presence of endometrial stem cell-derived conditional medium in healthy individuals in vitro.

Methods: Menstrual blood about 1-2 ml was obtained from healthy and endometriosis patients in the age range of 22–35. Endometrial-derived stem cells were isolated by Ficoll-Paque. After cell culture in DMEM containing 10% FBS, treating cells with conditioned medium from control group in passage three was performed. To determine the effect of conditioned medium derived from endometrial stem cells, the expression of stemness markers was evaluated by Real Time-PCR.

Results: In addition to the morphological difference seen in endometriosis-derived MenSCs compared with healthy MenSCs, stemness genes show different expression. The expression of OCT-4 and NANOG were increased in endometriosis-derived MenSCs under treatment for 4 days same as normal MenSCs. Also, SOX2 was showed similar expression after treatment but SALL4 was not showed significant difference.

Conclusion: Recognizing the changes of genes can provide therapeutic strategies for the endometriosis improvement. In addition to, change of expression of stemness markers in endometriosis patients in the presence of conditioned medium derived from endometrial stem cells can be an important strategy for treatment.

Keywords: Menstrual blood-derived stem cells, Endometriosis, Stemness genes, Condition medium

The effect of CRISPR-Cas9 gene editing on chromosomal damage of human embryos (Review)

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Introduction: CRISPR-Cas9 genome editing is a promising technique for clinical applications. In this study, computational pipelines to assess single-cell genomics and transcriptomics datasets from OCT4 (POU5F1)CRISPR-Cas9-targeted and Cas9-only were controlled human preimplantation embryos. This allowed us to evaluate on-target mutations that would be missed by more conventional genotyping techniques.

Methods: Ethics statement Human embryos were donated to the previous project by informed consent under the UK Human Fertilization and Embryo Authority (HFEA) License. CRISPR-Cas9 targeting of POU5F1 in vitro fertilized zygotes were microinjected with either a sgRNA-Cas9 ribonucleoprotein complex or with Cas9 protein alone and cultured for 5-6 days. The sgRNA was designed to target exon2 of the POU5F1 gene. Genomic DNA from Cas9 control and OCT4-targeted human embryos was isolated from either an individual single cell or a cluster of 2-5 cells from trophectoderm biopsies from embryos that developed to the blastocyst stage, as well as blastomeres from earlier stage embryos. Cytogenetic analysis To determine the chromosome copy number of samples, their genomic DNA was subjected to low-pass whole-genome sequencing. Libraries were prepared using the VeriSeq PGS Kit(Illumina)and sequenced with the MiSeq platform. PCR primer design and testing To independently investigate the prevalence of LOH events designed PCR primer pairs to amplify 15 fragments spanning a~20kb region containing the POU5F1 locus . also designed a control primer pair in exon 4 of the gene ARGFX, which is on a different chromosome. PCR amplification In preparation for PCR amplification and to expedite the processing of 2192 samples used the QIAgility robot for master mix preparation. The PCR reaction was run with the thermocycling settings. Targeted deep sequencing Clean PCR amplicons from the same DNA sample were barcoded and pooled to generate 137 barcoded libraries that were submitted for targeted deep sequencing by Illumina MiSeq v3(300bp paired-end reads). SNP-typing the MiSeq paired-end reads with DADA2 to remove low-quality regions trimmed. SNP calling was performed with BCFtools and call algorithms in multi-threaded mode. scRNA-seq data analysis scRNA-seq reads from G&T-seq samples were aligned to the human reference genome GRCh38 using TopHat2. selected samples for our scRNA-seq analyses are based on the quality of the eSNP-karyotyping profiles.

Results: Segmental losses and gains at a CRISPR-Cas9 on-target site identified by cytogenetics analysis The number of segmental and whole-chromosome abnormalities observed in the CRISPR-Cas9 targeted human cells was significantly higher than in the control samples(P = 0.0405). Moreover, this significant difference can be attributed to the observed segmental abnormalities on 6p, because

excluding them from the comparison results in a negligible difference in whole-chromosome abnormalities between targeted and control samples(P = 0.2419). Loss-of-heterozygosity identified by targeted deep sequencing data led to the identification of four different patterns: samples without LOH, that we're able to call heterozygous SNPs in multiple amplified fragments. Cases with putative LOH at the locus have heterozygous SNPs in the amplicons covering exons 1 and 5 of the POU5F1 gene(fragments E1-2, G1, and E4)and homozygous SNPs that could represent CRISPR-Cas9-induced deletions in the order of~4kb. Bookended samples have two heterozygous SNPs flanking the cut site but in fragments outside the POU5F1 locus and could represent deletions of lengths between~7kb and~12kb. Finally, in open-ended samples, it was not possible to find heterozygous SNPs in any of the amplified fragments or there was one or a few heterozygous SNPs on only one side of the region of interest that could represent large deletions of at least~20kb in length. No evidence of on-target complexity using digital karyotype and LOH analysis of the single-cell transcriptome data.

Conclusion: in contrast to Cas9 control embryos, a significantly higher frequency of CRISPR-Cas9 targeted embryos with a segmental gain or loss that was directly adjacent to the POU5F1 on-target site. LOH events may be overestimated.55.6% of CRISPR-Cas9 targeted cells did not exhibit any obvious segmental or whole chromosome 6 abnormalities and their genotype and phenotype, concerning the OCT4 function, are interpretable. Given the likelihood of mosaicism, it is unclear whether the segmental abnormalities we observed in any one cell analyzed from each embryo are representative of the entire CRISPR-Cas9 targeted embryo or a subset of cells within the embryo. overall, this points to the need to develop a robust technique to distinguish cells and embryos affected by CRISPR-Cas9 unintended damage from correctly edited embryos.

Keywords: CRISPR-Cas9, genome editing, chromosome, loss- of heterozygosity, human embryos

The effect of curcumin on the differentiation of dental pulp stem cells
(Research Paper)

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Introduction: Introduction: Tissue engineering and regenerative therapies are in progress in the treatment of dental problems, especially endodontics tratments. Induction of mineralization in dental pulp stem cells is of special importance. The aim of this study was to evaluate the effect of curcumin on differentiation of DPSCs by alkaline phosphatase gene expression and activation assessment.

Methods: Materials and Methods: In this study was assessed the toxicity levels of different concentrations of curcumin in 1, 2, 3 and 7 days by MTT assay. Alkaline phosphatase gene expression was determinded by Real Time-PCR and a specific kit was used to determine the alkaline phosphatase activity. Statistical analyses were performed using SPSS software version 17. Statistical significance was determined using t-test and ANOVA.

Results: Results: The results of the present study showed that curcumin did not show toxicity at low concentrations (0.5 µM). Also, gene expression and alkaline phosphatase activity in cells treated with curcumin for 7 days showed a significant increase compared to the control group ($p < 0.05$).

Conclusion: Conclusion: Considering the positive effects of curcumin on dental pulp stem cell differentiation and induction of alkaline phosphatase, this substance can be an intervention modality in bone and dental tissue engineering.

Keywords: Keywords: Dental pulp stem cell, Mineralization, Alkaline phosphatase, Curcumin, Gene expression

The effect of drug Ezetimibe in the treatment of Ebola (Research Paper)

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Introduction: In this article are paid to effect of drug Ezetimibe in the treatment of disease Ebola. As in article is called this drug disable this protein in the body is prevent treat disease. in fact this protein carry Ebola virus that by drug this protein disabled and can not carry the virus with your. In fact, this drug is a supplier of antigen to antibodies.

Methods: • As you know, the Ebola virus RNA virus in the family is Filoviridae. The virus then enters the body, and hemorrhagic fever is a disease that is fatal in 50 to 90 percent of patients will be symptomatic. Of course, from 4 species only leads to an asymptomatic infection and will not lead to death. Niemann-pick c1 receiver in research is absolutely essential for virus replication and traumatic. This receptor on hepatocytes and macrophages are actually located. This receptor as well entry cholesterol in these cells. In an article published so far, I found that only 10 percent survive of people patients with Ebola virus .I arrived at the conclusion that people rescued from the Ebola with hypercholesteromia protein that carries cholesterol in the name. I read many articles about the of Niemann pick c1 like 1. As well as the effect of Ezetimibe on the protein Niemann pick c1 like 1. In fact, according to this theory Ebola virus through the proteins Niemann pick c1 like 1 to the cells goal is transmitted through the receiver Niemann pick c1 enter cell and replication starts ,however, it should be noted that the protein Niemann pick c1 like 1 responsible for carrying cholesterol in the hepatitis and macrophages . In research on Niemann pick c1 like 1 protein was concluded that the protein is a protein in enterocytes of jejunum for absorption of cholesterol in the intestine is very important. In this theory people have hypercholesteromia of saved to be Ebola disease. because cholesterol with protein Niemann pick c1 like 1 connected and virus can not binding to protein Niemann pick c1 like1 and will be exposed to the antibodies.as mentioned protein Niemann pick c1 like1 carries cholesterol to hepatitis and macrophages. It should be noted that macrophages play a role in reverse cholesterol transport.

Results: if patients with Ebola be drug Ezetimibe due to disable the protein Niemann pick c1 like1, Ebola virus is exposed to antibodies .of course antibodies is most effective defense against Ebola virus.in fact ,Ezetimbe is a supplier of antigen in the body .Of course, in the last one research on the Ebola virus, Professor Pardis sabeti the Professor at Harvard university is acknowledged that study on the genes people rescued from the disease Ebola concluded these are people with Hypercholesteromia.

Conclusion: As explained in the article, it can be concluded that in patients with Ebola after receiving Ezetimibe drug due to the high affinity of this drug to the receptor Neiman pick c1 like 1 prevent the virus from entering the cell and thus cause visibility The virus will enter the immune system.

Keywords: : Ebola-NPC1L1-NPC1-Ezetimibe

The effect of exercise on pregnancy problems: A systemic study (Review)

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Introduction: Exercise is one of the most challenging stressors that requires the coordination of metabolic, respiratory and cardiovascular responses to meet the needs of muscles that are increasing energy. Today, all over the world, exercise is considered a necessity and everyone according to Exercises his own needs and lifestyle, for example: to lose weight, treat diseases and… . Every year, more than 600,000 pregnant women die due to pregnancy and childbirth problems. Exercise is one of the solutions recommended to pregnant women to reduce pregnancy problems During pregnancy, all non-contraindicated women are encouraged to exercise as part of a healthy lifestyle. Pregnancy is associated with increased empathy, which can be exacerbated by pregnancy conditions. Physiologically it is associated with the mother's cardiovascular, respiratory and metabolic systems that serve the needs of the developing fetus. Therefore, physiological adaptations to exercise during pregnancy are more pronounced and very important.the aim of this study was to investigate the effects of exercise on pregnancy problems

Methods: This article is a review article based on the collection of scientific materials from Iranian and English databases Google scholar-science direct-clinical key –magiran-springer ,Using Persian and English word search: exercise-pregnancy-depression-diabetes-blood pressure is among the articles of 2016-2018.

Results: According to studies Exercise during and after pregnancy had beneficial effects on reducing the symptoms and problems of pregnancy such as hypertension, low back and pelvic pain, urinary incontinence, physiological edema, weight gain, anxiety, etc. The results showed that exercise during pregnancy reduces the symptoms of depression. Recommending and promoting exercise and physical activity during pregnancy is a useful measure for women's physical and mental health. Low" to "moderate" quality evidence showed that prenatal pelvic floor muscle training (PFMT) with or without aerobic exercise reduces the likelihood of UI in pregnancy. Exercise was helpful in preventing the progression of UI in women with continental disease, but was not effective in treating UI in women with incontinence. Evidence of the benefits of combined exercise interventions [aerobic resistance + (muscle strength)] on maternal heart fitness and respiration and prevention of urinary incontinence was strong. For other interventions and outcomes, the level of evidence was found to be weak or insufficient. Low-intensity supervised exercise is safe for healthy pregnant women. Excessive pregnancy does not cause cardiac overload or affect the main outcome of pregnancy. Exercise during pregnancy can significantly control I improve heart autonomy . Aerobic exercise for about 30-60 minutes two to seven times a week during pregnancy, compared with sedentary lifestyle, is associated with a significant reduction in gestational abnormalities, gestational hypertension, and cesarean delivery. as well as aerobic exercise for 35–90 minutes 3–4 times per week during pregnancy can

be safely performed by normal-weight women with singleton, uncomplicated gestations because this is not associated with an increased risk of preterm birth or with a reduction in mean gestational age at delivery. Exercise was associated with a significantly higher incidence of vaginal delivery and a significantly lower incidence of cesarean delivery, with a significantly lower incidence of gestational diabetes mellitus and hypertensive disorders and therefore should be encouraged Exercise intervention can significantly reduce the risk of gestational diabetes, but showed no effect on gestational age at birth, preterm delivery, 2-hour glucose after OGTT, birth weight, and Apgar score less than 7. Aerobic exercise in overweight and obese pregnant women is also associated with significant prevention of gestational diabetes and should therefore be encouraged. Exercise during pregnancy can significantly reduce the incidence of GDM without reducing the gestational age at delivery and increasing the risk of cesarean section in women of normal weight.

Conclusion: As a result, pregnant women are encouraged to participate in safe and appropriate exercise, and it is recommended that pregnant women reduce their sedentary time as much as possible pregnancy is associated with decreased quality of life. These results suggest that it may be important for health care professionals to advise healthy pregnant women about the benefits of physical activity during pregnancy, as well as guidance on how to exercise during a healthy pregnancy

Keywords: Exercise , Pregnancy, sport, Maternal health,

The effect of human papillomavirus infection on the incidence and prognosis of squamous cell carcinoma of the tongue (Review)

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Introduction: Squamous cell carcinoma of the tongue(TSCC) is the most common tumor of the oral cavity and the second most common tumor in the head and neck area and one of the ten leading causes of death in the world. It can cause white and red spots on the tongue.Alcohol abuse ,smoking,and oral sex(oral infection), are risk factor for TSCC. Human papillomavirus is the most common sexually transmitted infection, which is also transmitted through skin contact and can cause warts in various parts of the body. Today, about 40 different strains of this virus can spread to the mouth, throat, and the penis, which in severe cases can cause a variety of cancers of the oral cavity or Cervix.

Methods: This review was performed within articles published at PubMed, Google scholar, Cochrane and SID from 1992 to 2020. The keyword were HPV , Tongue squamous cell carcinoma. By searching this database, 51 articles were found,24of them were not related with investigating and 15of them by reading abstract were removed. All articles chosen from English and Persian articles.

Results: Finally, 12 articles were included in the study. 2 articles definitely showed a positive relationship between the history of HPV and increased risk of TSCC, but did not mention a significant relationship between the history of HPV and tumor graid, stage or lymph node involvement.Three articles emphasized that smoking and alcohol consumption are very important cause of scc of the tongue, And hpv is considered to be the only possible factor for TSCC that the only way to prevention is to avoid risky behaviors such as (oral sex) and Vaccine injection.Another study showed that patients with TSCC who have a positive history of HPV have a better prognosis than those with a negative history of HPV,so that they did not need chemotherapy or radiation therapy or needed less invasive treatment. The role of hpv in the prognosis of other oral cancers is currently unclear.

Conclusion: Since human papillomavirus infection is known to be a risk factor for TSCC, other studies indicate a good prognosis for TSCC in the presence of HPV infection. Therefore, further studies in this field and counseling with sexual partners are recommended for help to prevention and treatment of TSCC.

Keywords: HPV , Tongue squamous cell carcinoma

The Effect of Humanized Cell Culture Media in Early Stage of Megakaryocyte Differentiation (Research Paper)

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Introduction: Hematopoietic Stem cells (HSCs) are small population of cell in bone marrow which can impaired for a different reasons, such as leukemia or tumors. HSCs transplantation is useful method for treatment this disorders. Umbilical Cord Blood (UCB) is a suitable source for this purpose. Number of HSCs in one unit of UCB is insufficient for a cell therapy so this can lead to a delayed or failed reconstruction of the cell and platelet recoveries. So it's necessary to generate megakaryocyte-committed cells for reduce period of platelet reconstruction and reduce high-cost, bacteremia, febrile reactions, and alloimmunization in allogenic platelet transplantation after HSCs transplantation. HSCs expansion in invitro need the cell culture media, which supplemented with FBS. FBS use has disadvantages such as limited resources, high cost and risk of xenovirouses transmission. Therefore, FBS should be replaced with products with human resources to reduce the risks of disease transmission and costs. Platelet lysates are a good source of enrichment for culture media. PL have different growth factors and cytokine, such as Insulin-like Growth Factor (IGF)-1, Platelet-derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Hepatocyte Growth Factor (HGF), which can improve cell proliferation and differentiation. The effect of PL on different cell lines as well as the differentiation of erythroid cells from HSCs has been studied, although so far no studies have been performed on the effect of platelet lysate on early stage differentiation of megakaryocytes.

Methods: The human umbilical cord blood was obtained from consenting parturients then Mononuclear cells (MNCs) fraction was separated within 8 hours after delivery and MNCs were enriched by Ficoll/Histopaque (density: 1.077 g/mL). CD34+ cells were isolated by positive selection using immuno-magnetic microbeads and MiniMACS columns. CD34+ cells were cultured in Iscove's Modified Dulbecco's medium supplemented with 10% PL or FBS, thrombopoietin, stem cell factor, Interleukin 6 and Interleukin 3 in 12-well plates. The cells were incubated in 5% CO2 humidified air at 37 °C for 3 days. Cells were harvested after 3 days from PL or FBS-containing media and megakaryocyte linage markers (CD41 and CD42b) and gene (GATA1, GATA2, FLI1, RUNX1) expression was assessed by flow cytometry and Real-time PCR, respectively. The cell expansion was also evaluated.

Results: Flowcytometry data showed expression of CD41 (16.34% and 13.51%), CD42b (5.12% and 3.46%), CD41/CD42b (4.22% and 2.67%) at the day 3 in cells cultivated in the PL containing medium and FBS containing medium containing media, respectively. RT-PCR results indicated increase GATA1, GATA2, FLI1, and RUNX1 gene expression in the PL containing medium than FBS containing medium. In addition, mean of 13 and 9 fold cell expansion were observed in PL and FBS containing medium, respectively.

Conclusion: In this study, we evaluated the effect of Platelet lysate substitution for Fetal Bovine serum in early stage of Megakaryocyte differentiation. CD41 and CD42 are related to megakaryocyte differentiation. CD41 is expressed in the early stage of megakaryocyte differentiation and CD42 is expressed in more mature megakaryocytes. In addition, some genes like GATA2, GATA1, RUNX1, and FLI1 are related to promote megakaryopoiesis and megakaryocyte markers expression. In our study, megakaryocyte markers and gene expression was increased in cells cultured PL containing medium than FBS containing medium. Additionally, cell expansion was increased in cells cultured PL containing medium than FBS containing medium. Our results showed that PL have not worrying about the transition of xenovirus and ethical problems and can be a suitable substitution for FBS in HSCs culture and differentiation into megakaryocytes. Although, the use of PL in HSCs culture and differentiation needs long-term cultivation and more evaluations.

Keywords: Platelet lysate, Fetal Bovine serum, Stem Cell, Growth Factor, Megakaryocyte

The effect of IL-6 gene expression on diabetes-related depression in patient for diabetes type 2 (Research Paper)

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Introduction: 2-type Diabetes is a Metabolic Disorder which Cause Hyperglycemia. Increased inflammatory cytokines Such as IL-6 can be associated with incidence of depression and type -2 Diabetes. Therefore, the above study investigated the effect of IL-6 gene expression on diabetes-related depression in patients with type 2 diabetes.

Methods: This study was performed on 50 patients with type 2 diabetes mellitus with depression and 50 patients type 2 diabetes without depression as control group. RNA extraction from Blood was performed by Yekta tajhiz kit and finally Gene expression assay was performed quantitatively using Real Time RTPCR and Nano drop.

Results: Interleukin 6 gene expression decreased in patients with type 2 diabetes with depression compared to those with type 2 diabetes without depression, which is not statistically significant.

Conclusion: The present study showed that decreased levels of interleukin-6 gene expression are not associated with post-diabetes depression. Therefore, more research is needed in this Field.

Keywords: Gene Expression - IL-6 - Diabetes Type 2 - Depression

The effect of Maternal Intravenous Hydration on amniotic fluid index in oligohydramnios (Research Paper)

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Introduction: Assessing amniotic fluid determines an important dimension of fetal health. The present study was conducted to determine the effect of maternal intravenous liquid therapy on amniotic fluid index (AFI) in oligohydramnios.

Methods: All the eligible women diagnosed with oligohydramnios were randomly assigned to an experimental group (n=31) (infusion of 3 liters of an isotonic Ringer's lactate solution within 24 hours) and a control group (n=30) (a constant-rate fluid infusion to keep vein open). AFI was measured in both groups before and 48 hours after the intervention. The patients, the sonographer and the person in charge of data analysis were blinded to the grouping of the women. Within-group differences were analyzed using the paired t-test and between-group differences using the t-test. $P<0.05$ was set as the level of statistical significance.

Results: The two groups of the women were matched in terms of age, parity, gestational age and birth weight of newborns. Forty-eight hours after completing fluid therapy, statistically-significant differences were observed in the mean AFI in the intervention group (4.06±0.33) and the control group (3.61±0.35) ($P<0.0001$) and also between the intervention group (0.532±0.45) and the controls (-0.036±0.18) ($P<0.0001$).

Conclusion: The results of the present randomized clinical trial suggested Maternal Intravenous Hydration significantly increases AFI in women with oligohydramnios. This treatment can be therefore employed to reduce maternal and fetal complications in oligohydramnios cases.

Keywords: Maternal intravenous Hydration, Amniotic fluid index, oligohydramnios

The effect of new compounds derived from metformin on Pseudomonas aeruginosa (Research Paper)

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Introduction: Due to the growing spread of resistance to classical antimicrobial agents, the innovative treatment method is necessary to struggle with antibiotic-resistant pathogens such as compounds derived from other drugs. Pseudomonas aeruginosa is one of the most important causes of nosocomial infections and has an innate resistance to a broad range of antibiotics. Metformin, a widely used anti-hyperglycemic, has a good safety profile, reasonably manageable side-effects, is inexpensive and causes a desirable amount of weight loss. Recent studies have shown the optimal effect of this drug on different bacteria. This study was performed to evaluate the antibacterial effects of metformin derivative (metformin and maleic anhydride) on Pseudomonas aeruginosa.

Methods: In order to increase the antibacterial activity and also to achieve new compounds, it was attempted to synthesize new derivatives of metformin. For this purpose, N, N-Dimethylimidodicarbonimidic diamide (metformin) was refluxed with maleic anhydride at 110 ° C for 30 hours to result in the presence of a new substance. Finally, the structure of the synthesized compound was confirmed by determining the melting point, C-NMR, H-NMR, TLC and IR. Then the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the synthesized drug on Pseudomonas aeruginosa were determined exerting microdilution and well method on Müller-Hinton broth and agar medium.

Results: Different colour and melting point and the results of C-NMR, H-NMR, TLC and IR indicate the new structure of the synthesized drug. The MIC and MBC of the metformin-derived drug on Pseudomonas aeruginosa were 0.75 and 1.5 mg/ml, and the inhibition zone was 10 and 13 mm.

Conclusion: The synthesized drug effectively has antibacterial activity Pseudomonas aeruginosa which can be used in pharmacy and treatment of infections caused by this bacterium.

Keywords: Metformin, Reflux method, Pseudomonas aeruginosa, Drug resistance, Antimicrobial effect

The Effect of Omega-3 Fatty Acid Supplement in Autistic patients (systematic review) (Review)

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Introduction: Introduction: Autism is a disorder beginning in childhood. It is marked by the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interest. Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual. More than 1% of newborns are affected by autism, a neurodevelopmental disorder. Brain has high level of lipid and omega 3 plays important rolls in brain. In this review we aim to investigate the effect of omega-3 fatty acids supplementation among patients with Autism Spectrum Disorders (ASD).

Methods: Methods: In this review, we include articles that discuss about the effect of omega-3 fatty acids supplementation among patients with Autism Spectrum Disorders (ASD). All articles were published between 1992-Sep 2020 and have ethical consideration and use human samples. We searched on PubMed, Google Scholar, science direct search engine with acute keywords: "autism","omega-3" and their variations which were obtained from Mesh. According to the keywords of the study, 221 articles were founded. 190 of them were excluded with considering the title; 15 articles were removed with considering the abstract. We use 16 articles at the end.

Results: Results: 16 clinical trial studies (n = 776) were reviewed. 12 articles reported improvement in some behavioral symptoms of ASD by using Social Responsiveness Scale (SRS) questionnaire. The p value of this study was below 0.05. But In 4 articles no significant changes observed and the p value of this study was above 0.05. So, most of the articles have stated that omega-3 may have a positive effect on the treatment of autistic patients.

Conclusion: Conclusions: we conclude from these articles that generally omega-3 acid fat improves symptoms in autistic patients, however, some researches does not show improvement. Answering this question enables neurologists to help patients suffering from autism. Of course, the few studies lead us to focus in this field more than previous. And until now in most of the studies on this topic have the low number of patients.

Keywords: Keywords: autism spectrum disorder (ASD), Omega-3

The effect of reducing oxygen concentration on mouse embryonic bi-cellular embryos and expression of Oct4 & Nanog genes (Research Paper)

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Introduction: In recent decades, assisted reproductive techniques have led to dramatic developments in the field of reproductive biology and infertility treatment. Many studies have shown that the introduction of environmental stresses affects the morphology and expression pattern of the embryo gene, and one of the goals of infertility clinics is to try to achieve culture conditions similar to those in vitro. The amount of oxygen that the embryo is in contact with during the early stages of development is one of these influential stresses. An increase in ambient oxygen levels increases the production of reactive oxygen species (ROS), which may be one of the possible reasons for the cessation of in vitro embryonic development in the two-cell stage. The use of incubators that provide less than 20% oxygen for embryo cultivation improves many quantitative and qualitative parameters such as embryo shape, viability, nesting, etc.

Methods: In this study, two-celled embryos after extraction were randomly divided into two groups. In the control group, embryos were cultured by applying ambient oxygen (20%) and in the treatment group, under hypoxia conditions (5% oxygen level), up to blastocyst stage. Then, in terms of cell, survival rate and exit from zona, and in terms of molecules, quantitative changes in the expression of Oct4 and Nanog genes were studied in both groups.

Results: The results of this study showed an increase in survival rate, exit from zona and also the expression of Oct4 and Nanog genes in the treatment group.

Conclusion: Environmental stress, nutrition and gas exchange during pregnancy play a very important role in the embryonic period.

Keywords: Blastocyst, Hypoxia, oct4 gene, Nanog

The Effect of Sinapic Acid Treatment on Acute Anxiety Behavior in Adult Male NMRI Mice (Research Paper)

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Introduction: Sinapic acid, a phenolic acid is a cinnamic acid derivative. The elevated plus-maze (EPM) and open-field test have broadly been used to investigate anxiolytic and anxiogenic compounds. The present study investigated the effect of sinapic acid treatment on acute anxiety behavior in adult male NMRI micein the EPM and open-field apparatus

Methods: . Animals were divided into five groups: control group and sinapic acid groups (5, 10 and 20 mg/kg, i.p.) and diazepam (0.75 mg/kg). During the test period, the number of open- and closed-arm entries, and the time spent in open of the EPM were recorded. Also, the anxiety behavior of animals was evaluated by open-field apparatus. Additionally, the GABA A/benzodiazepine (BDZ) mediation of the effects of sinapic acid was evaluated.

Results: Our results showed that administration of sinapic acid and diazepam significantly increased number of entries and time spent in open-arm of the EPM, whereas sinapic acid and diazepam significantly decreased number of entries and time spent in closed-arm of the EPM. The effects of sinapic acid in the elevated plus-maze were not altered by picrotoxin or flumazenil pretreatment.

Conclusion: The results of the present experiment indicate that sinapic acid may have an anxiolytic profile in mice behavior in the EPM and open-field test, which were not mediated by GABA A/BDZ neurotransmission.

Keywords: Sinapic acid, Anxiety, Mice, EPM

The effect of sonication on thyme essential oil- containing nano-niosome as nano bio-detergents (Research Paper)

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Introduction: Due to antimicrobial properties of plants, lots of attention has been recently paid to the addition of natural ingredients to pharmaceutical, food and healthcare systems. The aim of this study was investigation and synthesis of thyme essential oil - containing nanoparticles as bio-detergents.

Methods: Thyme essential oil was extracted and purified using Clevenger apparatus. Then nano -niosomes containing thyme essential oil was prepared by Bangham method using Tween 60, Span 60 and lipid cholesterol. Then, two methods were investigated in order to reduce the particles size (bath and probe sonication). The nanoparticles were characterized in term of release rate, size, zeta potential, morphology, infrared spectra and loading efficiency. The antibacterial properties of the detergent against E.coli were studied in term of the minimum bactericidal concentration (MBC), Minimum Inhibitory Concentration (MIC) and inhibition zone.

Results: The results showed a smaller particle size resulted from probe sonication compared to bath sonication. The essential oil loading efficiency of particles prepared by bath sonication was 5.56% higher than the probe sonication method. Type of sonication did not change the zeta potential of nanoparticles. The essential oil was physically encapsulated in the nano-niosome, without changing its properties during encapsulation. The nanoparticle was uniformly disturbed with spherical structure. The results showed a significant anti-bacterial property of the detergents against E.coli (MBC of 31.25µg/ml).

Conclusion: Bath sonication is economically recommended compared to probe sonication in preparation of nanoparticles. The results of this preliminary study introduce an anti-bacterial herbal detergent which can be more developed in further studies.

Keywords: Noisome, Herbal detergent, Zataria multiflora, Anti-bacterial, E.coli.

The effect of terhalose on the removal of beta-amyloids (Review)

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Introduction: Trehalose is a nonreducing disaccharide that naturally available (found in diverse organisms such as plants, bacteria, yeast, fungi, mushrooms and insects). In many neurodegenerative disorders like Alzheimer's, Parkinson's, or Huntington's disease, it was found that abnormal aggregation and deposition of specific proteins occurs

Methods: From the studies and articles we have examined, we have concluded that Terhalose also has a chaperon- like activity and the ability to modulate inflammatory responses has also been reported.

Results: Numerous studies have proven that Trehalose limits these processes and the inhibits formation of neurotoxic amyloids. Trehalose may be used in drug design procedures. it may be used in drug encapsulation because it is non-toxic and effective in formation of neurotoxic in certain disorders. It has a chaperone-like activity, prevents protein misfolding or aggregation, and by promoting autophagy, contributes to the removal of accumulated proteins (B amyloid).

Conclusion: trehalose can activate autophagy via PI3K/Akt/mTOR, AMPK/ULK1/ mTOR, Bcl-2/Beclin-1, and TFEB pathways.These pathways regulate authophagy eukaryotic cells.

Keywords: Trehalose,B-amyloid,Autophagy

The effect of the hematopoietic stem cells (HSCs) aging in human life span (Review)

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Introduction: Novel blood cells are constantly generated from the hematopoietic stem cells (HSCs), which inhabit in the bone marrow (BM). During the life-span of the organism, this stem cell storage protects life. However, HSCs can persevere in vivo prolonged than one longevity, with senescent, HSC regenerative capability reduces and skewing from lymphopoiesis toward myelopoiesis happens. In addition, the increase in the senescent HSC pool prepares adequate, yet unusual, blood generation. Here we review our current understanding of the molecular mechanisms that contribute to HSC aging. Age-dependent alterations in HSC are included to DNA damaged, the epigenetic landscape, and metabolic stress. As many hematological pathologies are powerfully age-related, strategies to intervene in aspects of the stem cell aging process may have significant clinical relevance.

Methods: In this review we used online database such as NCBI (PubMed), and Google scholar. This Research is the result of a survey of more than 175 articles of which 113 articles are directly used in this study.

Results: As discussed in this review, studies have pointed toward intrinsic deficiency in HSC function, and epigenetic dysregulation as main contributing factors behind HSC reduction and malignancy during senescent. Gene expression investigations and as well as mouse models demonstrate that DNA modification pathways and preservation of genomic resistance could be one of the cause arose for aging in HSCs. Damage of epigenetic regulation possible account for those aberrant gene expression seen throughout senescent.

Conclusion: Many important pathway and molecular function in young and aging HSCs are unknown. Thus, further studies are necessary to pinpoint this relationship and how it changes during aging. However, recently study of the molecular regulation of stem cell function and the mechanisms that go awry during aging is rapidly expanding due to technological advances such as identification of aging markers. Accordingly, future studies will elucidate the inter-play among these possible mechanisms. Via excellent comprehension HSC senescent we can be able to improve the damage of regenerative capability of elderly HSCs.

Keywords: HSCs, Aging, DNA damage, Epigenetic, Metabolism

The effect of weightlessness on progesterone receptor gene expression changes in Triple negative breast cancer cell line (Research Paper)

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Introduction: Spaceflight and ground-based weightlessness analog experiments have suggested that gravity can affect cell growth, metabolism, morphology, development, and gene expressions (1, 2). Alteration on properties of different cell lines such as cancer cells or stem cells under weightlessness was reported in several studies (3, 4). In this study, we evaluated the alteration of progesterone receptor gene expression in human triple-negative breast cancer cells after 1 and 3 days of exposure to weightlessness conditions.

Methods: MDA-MB-231 is triple-negative breast cancer (TNBC) cell line as it lacks estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2)(5). The cells were cultured in Dulbecco's modified Eagle medium (DMEM), containing 10% sodium bicarbonate, supplemented with 10% fetal bovine serum (FBS), and penicillin (50 IU/ml)/streptomycin (50 µg/ml). All cell lines were incubated at 37°C in a humidified incubator with 5% CO2.in order to simulating microgravity, two-dimensional clinostat was employed. Cells were cultured at culture tube (TPP, Switzerland) and after the cells stick, tubes were completely filled by the medium. The rotation times were 1 and 3 days and the device rotated by 30 rpm. Total RNA was isolated from the lysed cells and was subjected to reverse transcription using the qScript™cDNA Synthesis kit. To analysis, the gene expression using Quantitative real-time RT-PCR, primer sequences were as follows: PR-total F (5'AGCCCACAATACAGCTTCGAG3'), PR-total R (5'TTTCGACCTCCAAGGACCAT3') (6). As a positive control, glyceraldehyde-3-phosphate dehydrogenase mRNA (GAPDH) was amplified in parallel with the primers: GAPDH F (5'ACGACCACTTTGTCAAGCTCAT3') and GAPDH R 5'TCCACCACCCTGTTGCTGTA3'). Cycling conditions were: 95º C for 30 sec; followed by 40 cycles of 95 ºC for 20 sec and 95 ºC for 40 sec. Melting curve analysis was performed for each gene and changes in the fold number were calculated by using the 2ΔΔCt method. A statistical correlation was performed using independent samples t-test and $p<0.05$ was considered statistically significant. Relevant diagrams were drawn using the Graphpad Prism 7 programs.

Results: Results and discussion Gravity is one of the most important mechanical factors on earth that has immense effects on living organisms. Every change in an organism is affected by changes in its cells. However, information on the effects of no gravity on the gene expression is very low. Thus, simulated microgravity may be used as a novel methodology for manipulating cells along with other biochemical techniques. To investigate the effects of weightlessness, a simulator was used. After 1 and 3 days exposure to microgravity conditions, the RNA was extracted from cells and the cDNA were constructed. After that, a real-time PCR method was employed for investigation progesterone receptor gene alteration. No significant changes in gene expression were observed. On the other hand, microgravity had

no effect on the progesterone receptor gene on MDA-MB-231 breast cancer cell lines.

Conclusion: The result proved that weightlessness has not detectable influence on the gene expression of progesterone receptor in MDA-MB-231 cells at transcriptional levels, suggesting that there is a strong transcriptional control of this gene or optimization of microgravity application time may yield better results. Collectively, these results demonstrate that further studies may be necessary and investigation on protein level may yield other interesting results.

Keywords: weightlessness, triple-negative breast cancer cell line, progesterone receptor

The effective material from of the Caryophyllaceae family for the treatment of acute respiratory diseases, especially COVID-19 (Research Paper)

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1.

Introduction: The purpose is to make a medicinal plant using the plant family Caryophyllaceae.Following the outbreak of SARS in 2003, human coronavirus (HCOVS) was reported as a pathogen. They cause severe symptoms in respiratory infections.Coronaviruses are a large family of viruses and subspecies of coronaviruses that range from the common cold virus to the causative agent of more serious diseases such as SARS, MERS, and Covid-19. The glycoproteins is due to the entry of the cell that is the main cause of tropism (which represents the biological agent of and organism) and the host tropism and the tissue that targets the pathogen.

Methods: this virus has RNA and ribosome and transcription have caused this disorder. And this active ingredient has a positive effect on the ribosome, and most importantly, it is effective for the trachea and bronchi.

Results: This active ingredient is used in the manufacture of drugs and vaccines for respiratory diseases and a variety of coronary viruses, especially COVID 19

Conclusion: _Effective treatment of COVID 19 _Increased immune system

Keywords: covid19,Caryophyllaceae,Coronaviruses ,diseases,drug,glycoproteins

The effectiveness of massage to the first stage of labor: A systematic review (Review)

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Introduction: Labor is identical to the pain that will be experienced more than 90% of women experience severe labor pain and it is a challenging issue for nurses designing intervention protocols. Labor pain was an emotional experience and involves both physiological and psychological mechanisms during labor. Effects of labor pain includes inflammation in uterus and labor dystocia. Nowadays, the use of analgesics for pain relief in childbirth is rarely used due to maternal and neonatal complications and the non- pharmacological and complementary medicine methods are increasing. One of an effective non pharmacological method to reduce pain and anxiety is with massage. This study is to determine the effectiveness of massage to the first stage of labor.

Methods: In this study all papers from 2016-2020 were identified in a search of Elsevier, PubMed and SID, Google Scholar databases. Finally 70 studies that evaluated the effectiveness of massage to the first stage of labor.

Results: The findings of this systematic review suggested that massage therapy can reduce labor pain intensity. Circular manual massage, counter-pressure massage at lumbosacral region, endorphin massage, Circular Hip and knee Press massage, acupressure, effleurage, abdominal lifting technic, slow stroke back massage, Foot reflexology, Oketani massage, kinesio taping, Court-type Thai traditional massage, massage with strong strokes, rubbing or stroking (twisting and releasing) during the active phase of labor could decrease the intensity of labor pain, duration, maternal complications and increase uterine contractions. Massage stimulates the body to release endorphins can also reduce anxiety. Massage therapy is more effective and efficiency reduces pain on stage 1 of vaginal delivery when combined with breathing techniques and relaxation and ice pack application or heat therapy techniques. Using lavender oil, frangipani oil, jasmine oil, olive oil, almond oil, ginger oil, sesame oil massage have the greatest effect in reducing pain.

Conclusion: The study finding shows the importance to provide massage as a cost-effective intervention for reducing labor pain among the pregnant women and suggests this non-pharmacological method replace the methods of drugs that can positively influence the quality of women's birth experiences. The results of this study are expected to enrich and contribute to the development of science in the field of health promotion, and serve as an additional input for midwives in order to carry out the care of mother during labor.

Keywords: massage, labor, pain, anxiety

The effectiveness of training based on the theory of planned behavior on the choice of type of delivery; A review article (Review)

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Introduction: Over the past decade, an unprecedented and continuous increase in the rate of cesarean has caused Controversy and concern among experts, health caregivers and politicians. Reducing the rate of cesarean with the aim of improving the health indicators of mothers and infants is one of the goals of the health system evolution plan. In many cases, only medical reasons do not determine the type of delivery, Awareness, beliefs, behaviors and misconceptions about natural delivery are also decisive. One of the most important theories of predicting and understanding behavior is the theory of planned behavior (TPB). The aim of this study was determination the effect of education based on the theory of planned behavior on the Selection of type of delivery in pregnant women.

Methods: This review study articles on the related topic (Education, theory of planned behavior , delivery, pregnancy) were searched in the following databases Google scholar, SID, Magiran , Iranmedex , Scopus, PubMed, Science direct. A total of 13 related research papers, between 2010 – 2020 were included in this study.

Results: The result of the study showed the main reasons for selective cesarean delivery are low level of knowledge and attitude about normal delivery. One of the most effective factors in predicting the choice of delivery method was the subjective norms and perceived behavioral control. So in the women that subjective norms supported natural delivery and had high perceived behavior control were more likely to choose natural delivery than other women. The results of this study showed the effectiveness of training based on the theory of planned behavior on the structures of attitude, perceived behavioral control, subjective norms and behavioral intention related to the selection of delivery method.

Conclusion: Designing an educational intervention based on the structures of the theory of planned behavior can be an effective strategy to change the positive perceptions of pregnant women about cesarean delivery and ultimately reduce the intention of cesarean delivery.

Keywords: Education, theory of planned behavior , delivery, pregnancy

the effects of aerobic exercise and ginseng supplement on weight and sperm parameters in obese rats (Research Paper)

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Introduction: aerobic exercise is one of the factors affecting the health and secretion of body hormones. Changing lifestyle and decreasing physical activity is one of the causes of impotence and increasing infertility in society. The aim of this study was to compare the sperm parameters and sex hormones in rat who were undergoing aerobic training and to compare with rat who did not receive these exercises.

Methods: Thirty-tow male Sprague Dawley rats (weighing 200 to 260, 4 months old) were randomly divided into aerobic exersise, ginseng, ginseng and aerobic exercise and control groups (n = 8). Exercise program It consisted of eight weeks of aerobic exercise on a treadmill (five sessions) Meetings per week, 30 minutes per session, fast 22m / min and 5% slope). After eight weeks of aerobic training and ginseng consumption, the mice were anesthetized in separate groups and blood samples were collected.also Stabilization, processing, incision of testicular tissue and finally staining steps were examined by hematoxylin and eosin (H&E). Sperm quality was calculated based on Johnson method. Data were analyzed using independent t-test and a significance level of $p < 0.05$ was considered.

Results: Evaluation of the hormones of the participants showed that the mean levels of testosterone, LH, FSH and prolactin in the treated group were 3.66 /1 1.20, 4.95 /2 2.23, 9.33 4 4.22, respectively. In the control group were 13.02 3 3.57 which were 5.50 5 5.13, 6.09 /2 2.44, 9.54 5 5.60 and 64.42 13 13.36, respectively. Which indicates that these exercises are effective on the hormonal index of individuals. The results also showed that the spermogram indices of the rats under exercise were significantly better than those in the control group who did not.

Conclusion: The results of this study showed that aerobic exercise, physical activity and ginseng can greatly help to restore fertility and prevent impotence.

Keywords: Keywords: aerobic exercise, Infertility, Sperm, Fertility

The effects of increasing plasma cholesterol concentration in high-fat diet of mothers on plasma concentrations of immunoglobulin M and G in male and female neonates of rats. (Research Paper)

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Introduction: No living thing can survive in its environment without a proper immune system. Animals must defend themselves against microorganisms to survive.Considering the importance of the immune system in maintaining the life of the body therefor there is the nessecity to study the effect of pregnant mother's diet on the newborn's immune system

Methods: In this experimental study, 40 female rats and 20 adult male rats were used.Control group without special treatment, (average cholesterol 2 weeks), (average cholesterol 6 weeks), (high cholesterol 2 weeks), (high cholesterol 6 weeks).After the end of the high-fat diet before pregnancy until the end of breastfeeding Male and female neonates were sampled separately gG and IgM concentrations were measured, then data were analyzed by SPSS software. In all cases, $p \leq 0.05$ was considered as a statistically significant level.

Results: The groups (high cholesterol 2 weeks) and (high cholesterol 6 weeks) decreased the mean IgG concentration compared to the control groups (average cholesterol 2 weeks) and (average cholesterol 6 weeks) The groups (high cholesterol 2 weeks) and (high cholesterol 6 weeks) decreased in the mean IgM concentration compared to the control groups, (average cholesterol 2 weeks) and (average cholesterol 6 weeks).

Conclusion: Consumption of high cholesterol by mothers has reduced IgG and IgM levels in male and female rats.

Keywords: High cholesterol, immunoglobulin, neonatal rats

The Effects of intraperitoneal injection of Acesulfame-K on sperm motility and morphology in rats (Research Paper)

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Introduction: Acesulfame-K (Ace-K) is one of the most potent sweeteners with many applications. The aim of this study was to investigate the effect of intraperitoneal administration of Acesulfame-K during pregnancy on sperm in male offspring.

Methods: : Four groups of rats were intraperitoneally injected with Ace-K in doses of 50, 100, 200 and 400 mg/kg body weight during pregnancy. The control group received 0.5 ml of normal saline. After the lactation period, male newborn rats in each group were separated from their mothers and divided into two groups: treated group which received Ace-K as their mothers had and untreated group which reached puberty naturally. After anesthesia a number of rats in each group were then dissected and sperm samples were obtained from the epididymal tail. Sperm density, morphology, and motility were evaluated. The offspring testis weight to body weight ratio were also examined.

Results: There were no significant differences in sperm density and in testis weight to body weight ratio compare with control group. A significant difference in the percentage of abnormal sperm was observed in both groups in the 50mg dose. A significant decrease in sperm motility was observed in the "treated group" with 200 and 400mg doses, and significant increase was seen in the "treated group" with the 50 and 100mg doses and the "untreated group" with the 400mg dose.

Conclusion: Considering the effects of potassium acesulfame on sperm motility and morphology, it is necessary to study the fertility of rats treated by this artificial sweetener in future research.

Keywords: Acesulfame-K; Male rat; Sperm; spermatogenesis.

The effects of preterm feeding on infants(Systematic review) (Review)

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Introduction: The role of Complementary nutrition is important in the month. Supplemental Nutrition means the use of different pyramid groups for the growth and health of the child, which is important after six months. Paying attention to the right time to start supplementary nutrition is one of the most important elements in a baby,s growth and development. Considering the importance of timing of supplemental feeding in a child,s health, this study was designed to investigate the early onset of complementary feeding.

Methods: This review was performed within articles published at PubMed, Google scholar, Magiran and SID from 2000 to 2019. The keywords were Early feeding,supplementah nutrition,infant . By searching this database, 62 articles were found, 26 of them were not related with investigating and 11 of them by reading abstract were removed. All articles chosen from English and Persian articles.

Results: According to the findings of the articles most developmental disorders occur in the first year of life of the infant, especially after the end of the exclusive period of breastfeeding ,when infant needs a lot of nutrients on the one hand and on the other hand there are limitations in the quality and quantity of diet. Often infants grow well up to the age of six months, while in the second six months the infant's body reserves more or less decrease. Therefore, the importance of starting complementary feeding at this age becomes apparent. The important point is the time to start complementary feeding, so early feeding children not only did not affect their growth and development, but also led to disease and weight loss.

Conclusion: The end of six months is the best time to start developmental feeding after six months of exclusive breastfeeding. It is wrong to start complementary feeding early because the gastrointestinal tract is not ready. On the other hand, early initiation of complementary feeding causes less sucking of the mother's breast, which is one of the important factors in reducing breast milk production. Also, the biggest risk of early supply of evolutionary foods is diarrheal diseases. Therefore, it is suggested that educating mothers not to start early feeding is one of the components of future research.

Keywords: Early feeding , Complementary nutrition, Infant, six months

The Effects of Psychological Interventions on Menopausal Hot Flashes: A Systematic Review (Review)

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Introduction: Menopause is just a normal physiological phenomenon, closely identified with a great deal of physical-psychological symptoms, including hot flash (HF) with a prevalence rate of 20-80. Therefore, various pharmacological and non-pharmacological interventions have been thus far practiced to reduce this common symptom of menopausal transition. This systematic review was fulfilled to evaluate the effects of psychological interventions on menopausal HFs.

Methods: In this review, the databases of Google Scholar, Scopus, PubMed, Web of Science, Science Direct, the Cochrane Library, and Scientific Information Database (SID) were searched applying the Boolean Searching Operators as well as the keywords of “hot flashes”, “menopause”, “psychological intervention”, and “vasomotor symptoms”. Accordingly, a total number of 20847 articles completed during 2000-2019 were retrieved. After excluding the duplicate and irrelevant ones, the quality of 19 clinical or quasi-experimental clinical trials was assessed via the Jadad scale.

Results: The interventions implemented in the studies on menopausal HFs included cognitive-behavioral therapy (CBT), mindfulness-based stress reduction (MBSR), hypnotherapy, and relaxation techniques. According to this review, all the articles had reported improvements in HFs in postmenopausal women, except for four studies. Moreover, six of the 19 articles had an acceptable quality, with reference to the Jadad scale.

Conclusion: Based on the results of the articles examined, most psychological interventions could boost menopausal HFs.

Keywords: Menopause, Hot Flashes, Hot Flash Symptoms, Psychological Interventions, Psychotherapy

The effects of TiO2 nanoparticles and its photocatalytic on Candida albicans (Research Paper)

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Introduction: Candida albicans is the fourth common cause of chronic fungal infections that cause both mucosal and deep tissue infections. Metal oxide nanoparticles are known to possess strong antimicrobial properties. Titanium dioxide (titania) nanoparticles have a wide range of antifungal as well as biomedical applications. In the present work, the antifungal properties of Titanium dioxide nanoparticles were investigated using Candida albicans.

Methods: In this study, The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MFC) of nanoparticles of Titanium dioxide were determined using a good assay method.

Results: In this experimental study, the MIC of photocatalyst TiO2 nanoparticles was 2.5 µg / ml while MFC was determined to be 3.5 µg / ml.

Conclusion: photocatalyst TiO2 nanoparticles showed a suitable antifungal property against C . albicans The present study showed that Titanium dioxide nanoparticles can be used as a deterrent against the pathogens of the materials and avoid contamination.

Keywords: nanoparticles, Candida albicans , antifungal

The Evaluation of antimicrobial effects of esfand (Peganum harmala) and lavender (Lavandula angustifolia) (Research Paper)

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Introduction: Herbal medicine is the art and science of using herbs for promoting health and preventing and treating illness. It has persisted as the world's primary form of medicine since the beginning of time, with a written history more than 5000 years old. A number of scientific investigations have highlighted the importance and the contribution of many plant families as medicinal plants. Medicinal plants play a vital role for the development of new drugs. The aim of this study was the assessment of antimicrobial effects of esfand (Peganum harmala) and lavender (Lavandula angustifolia) extractions on Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicans.

Methods: Extracts of the plants were prepared by using Soxhlet extractor. Disk diffusion assay was used to evaluate the antimicrobial effect and for determining the minimum inhibitory concentration (MIC), the broth microdilution method was performed. The effect of each extract was compared with conventional antibiotics against all these pathogenic microorganisms

Results: The results showed that both of the extracts had antimicrobial activity. Staphylococcus aureus was more sensitive to methanolic extract of esfand (34.33 mm) than Pseudomonas aeruginosa. The effect of these extracts on gram positive bacteria was significantly higher than gram negative bacteria. The results also revealed both extracts had antifungal effects.

Conclusion: According to this study, it is clear that methanolic extracts of spand and lavender have a significant antibacterial and antifungal effect against pathogenic bacteria and Candida albicans, Therefore, this extract can be considered as a natural herbal product for controlling bacterial and fungal infections.

Keywords: Peganum harmala, Lavandula angustifolia, Antimicrobial, Disk diffusion, pathogenic microorganisms

The Inhibition Effect of Lactobacilli Against Growth and Biofilm Formation of Pseudomonas Aeruginosa Isolated from Burn Patients (Research Paper)

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Introduction: Today, probiotic bacteria can be used as safe and suitable candidates for the prevention of pathogenic bacterial infections. They produce antimicrobial components and compete with pathogens for host cell receptors. The present study aimed at evaluating probiotic lactobacilli antagonistic and antiadhesive activities against multi-antibiotic resistant Pseudomonas aeruginosa isolated from burned patients.

Methods: This study examined 100 strains of multidrug-resistant (MDR) P. aeruginosa isolated from patients, who were admitted to the burn units of hospitals. Antimicrobial activity of L. casei and L. plantarum against P. aeruginosa was determined by a modified double layer and well diffusion methods. Anti-adhesive effect of two probiotic lactobacilli and co-aggregation assay were determined by microtiter plate method. Finally, expression of two main adhesion genes, algD, and pelA was investigated in 100 MDR P. aeruginosa isolates via real-time polymerase chain reaction (RT-PCR) assay.

Results: The results of the present study, 97 of 100 isolated P. aeruginosa had the algD gene and all of them had pelA gene. The lactobacilli bacteria were showed good inhibitory effect on P. aeruginosa especially on algD and pelA expression. Co-aggregation between L. casei and L. plantarum with P. aeruginosa was 44.8 and 37.3%, respectively. The average of the anti-adhesive effect of L. casei and L. plantarum supernatants on P. aeruginosa was obtained as 51.9 and 42.1%, respectively.

Conclusion: Probiotic lactobacilli can be a new suitable candidate for controlling P. aeruginosa infections.

Keywords: Anti-adhesive, antimicrobial, Pseudomonas aeruginosa, probiotic lactobacilliو Real Time PCR.

The Inhibitory Effect of Let7 on Metastasis of Breast Cancer Cells (Review)

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Introduction: MicroRNAs(the group of small RNAs with 19-25 neucloids) are one of the largest classes of post-transcriptional regulators which designate a small portion of the genome. They control gene expression in different biological processes, and it has been proved that microRNAs are also associated with cell cycle regulation, metastasis, apoptosis, etc. Second, microRNA to be found was the one named Let7 in year 2000.Metastasis is the action in which cancer cells migrate through the body and start to grow in distant new locations, and breast cancer is a type of cancer that develops from breast tissue in which growth and division of some breast cells are much faster than normal ones.

Methods: This article is a review article in which the total investigation, included 26 articles located in databases including Web of Science, PubMed, and Google Scholar (P value < 0.005)

Results: As microRNAs play a precise role in carcinogenesis, studying changes in microRNA expression in cancers and other human malignancies is critical. It is evidenced that Let7 cluster is mostly downregulated in tumors of the breast and also lungs and thyroid; therefore, increasing levels of Let7 can have an inhibitory effect on metastatic tumors like breast cancer cells.

Conclusion: In order to upgrade the survival of cancer patients, it is essential to improve treatment of metastasis because it has been the main cause of cancer mortality for years. Huge potential of microRNAs for therapeutic applications in cancer is also evidenced because they are so stable that they can be easily detected in serum of cancer patients, and it can be concluded that by paying attention to the significant role of Let7 in association with metastasis, we can say that it can be an appropriate candidate for curing breast cancer.

Keywords: Let7, cancer, MicroRNA, metastasis

The key miRNA Biomarker panel of pancreatic ducal adenocarcinoma (Research Paper)

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Introduction: Cancer is one of the most destructive diseases Gastrointestinal (GI) cancers are among the most prevalent and lethal tumor globally. Statistics showed that each year, of the 18 million diagnosed universally, about 500,000 cases were pancreatic. Pancreatic ductal adenocarcinoma (PDAC) is the most prevalent type. It is considered as the fourth leading cause of cancer death. The poor specificity and sensitivity of PDAC's biomarkers in conventional clinical purposes seems to be one of the major obstacles in this illness MicroRNAs (miRNAs), considered to regulate the activity of approximately 30% of all protein-coding genes in mammals aberrant expression of miRNAs as the small non-coding RNAs have been identified as a potential appliance for early diagnosis, prediction of treatment response, and prognosis of patients with PDAC. In this study, we aimed to collect all microarray data which is related PDAC gene expression and drawing protein-protein interaction networks to found the correlation of final genes Moreover, pathway analysis was performed to clarify much more important biological pathways in PDAC develops

Methods: datasets of pancreatic ductal adenocarcinoma were searched using the keywords: 'pancreatic ductal adenocarcinoma, 'Homo sapiens' and 'Expression profiling by array' against the Gene Expression Omnibus (GEO) database (http://www.ncbi.nlm.nih.gov/geo). To identify differentially expressed miRNA, each dataset was analyzed by limma R package in Bio conductor. Significant differential expression was determined as a log fold change ≥ |2| and adjusted p-value threshold of 0.001. To find the hub target genes, draw gene-miRNA Interaction network and report the hub targeted genes

Results: After a systematic review, 4 GSE profiles from 9 datasets (GSE109918 , GSE101094, GSE89139, GSE41369) which totally include 47 cases, were included. To the evaluated quality of data. Heat map and principle Component Analysis (PCA) was performed. Based on logFC and target genes which were summarized in table. As Up-regulated candidates miR-155, miR-221, miR-222 and miR-126, miR-193b, miR-106b as down-regulated miRNA, respectively

Conclusion: About the poor prognosis of pancreatic cancer in human societies, understanding the events and molecular pathways, as well as taking early health strategies with an emphasis on biological markers is very important. Recent researches on epigenetic mechanisms have shown that regulatory features are involved in the development, progression, and metastasis of pancreatic cancer. For example, the mir-1290 has a dedicated function and is a good alternative to the CA19-9 marker. This biomarker is very important for screening people who have a family history of pancreatic cancer. Also, mir-373 is very effective in the process of metastatic pancreatic cancer

Keywords: pancreatic ductal adenocarcinoma, miRNA expression, Bioinformatics,

The major role of Interleukin-6-174G>C gene polymorphism in prognosis of different cancer types (Review)

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Introduction: introduction: The cancer prognosis influenced by the cancer type, stage of tumor and nominated treatment choices. Primary identification and precise prognosis prediction is foremost issue in cancer managements. In this regards, Inflammation has a very vital contribution to cancer progression since malignant cells are certified by the inflammatory cytokines in a microenvironment are to be extremely proliferative. Interleukin-6 (IL-6) has a key factor in inflammation which is engaged in the cancer development pathogenesis. IL-6-174G>C polymorphism and its impacts on protein and gene expression of IL-6 has been revealed in abundant surveys.in this study we focused on the main role of interleukin -6-174G>C gene polymorphism in cancerous affected subjects.

Methods: Methods; : As a theoretical study, our extracted date were obtained by searching cancer , inflammation , and 174G>C gene polymorphis keywords in Science direct, Pubmed and Scopus websites in relations of content .This items was written according to preferred articles.

Results: Results ; In this regards association between IL-6-174G>C polymorphism and overall survival (OS) of cancer by qualified surveys with various patients involved. Studying different Meta-analysis exhibited that IL-6-174G>C polymorphism is and not related to OS but evaluated by innumerable genotype comparison for instance; GG/(GC+CC), CC/(GC+GG) and CC/GG. Former studies display that, individuals with IL-6-174GC genotype had decreased hazard of poor OS versus GG. Nonetheless, for GG/(GC+CC) genotype assessment, this SNP is affect subjects' OS apparently in some neoplasms, nonetheless pooled outcomes presenting negative relationships since contrary and protective impact on innumerable type of cancer balance each other.

Conclusion: Conclusion : Overall it could be concluded that IL-6-174G>C polymorphism might has imperative role in controlling OS in several cancer types comprising CLL and might associated with patients treatment in the future.

Keywords: polymorphism , interleukin 6, genotype

The Marine Brown Algae compounds; the natural Antidiabetic sources (Review)

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1.
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Introduction: Marine algae are known sources of bioactive metabolites. Diabetes mellitus is a metabolic disorder and one of the first death causes in the world. Due to the various antidiabetic drugs side effects, finding an effective natural-based antidiabetic drug is a desire. Phlorotannins present in marine brown algae is one of Antidiabetic compounds which operating through different mechanisms such as the inhibitory effect of enzyme targets mainly by inhibiting the Enzymes. Most of the impressible enzymes such as α-amylase, α-glucosidase, angiotensin-converting enzymes (ACE), aldose reductase, dipeptidyl peptidase-4, and protein tyrosine phosphatase 1B (PTP 1B) enzyme are the ones which get effected by Phlorotannins. one of the main therapeutic interventions to treat type 2 DM is achieved by postprandial hyperglycaemia Reduction [14]. The carbohydrate-hydrolysing enzymes such as α-amylase and α-glucosidase can cause the Postprandial hyperglycaemia reduction. Therefore, the inhibition of such enzymes leads to the reduction of postprandial blood glucose level and these enzyme inhibitors act as a potential target for the development of antidiabetic drugs.

Methods: The other natural compounds identified in brown algae are effected on glycation cycle. The final products of glycation cycle which made by Chronic hyperglycaemia in diabetic patients have caused of vascular complications in diabetes, renal failure, Alzheimer's disease, aging, and other chronic diseases. Therefore, the natural compounds which inhibit the glycation final products formation can be used to suppress the diabetic complications associated by glycation end products accumulation.

Results: In addition there are some polysaccharides Present in Marine Brown Algae which made by phlorotannins such as fucoidans, alginates, and laminarans. Based on researches laminarans have effective therapeutic effects. Fucoidans show antioxidant, antidiabetic, and anti-inflammatory activities and Fucoxanthin exhibits strong biological activities such as antioxidant, anticancer, and antidiabetic activities. also , based on researches six subgroups of phlorotannins are identified in different species of brown algae, which show important antidiabetic action through several mechanisms. Due to the results there are six groups of compounds which brown algae have effected on them such as α-Amylase and α-Glucosidase Enzymes, Aldose Reductase, Angiotensin-Converting Enzymes, PTP 1B, DPP-4, AGEs.

Conclusion: Brown algae known as a great source of bioactive compounds. One of the considerable health-promoting compound have achieved is phlorotannins. Phlorotannins is an antidiabetic agentidentified in the brown algal species . Among the vast brown algal species a few numbers have suitable to use as antidiabetic s sources. During these years the families such as Lessoniaceae, Ishigeaceae,

Sargassaceae, Fucaceae, Laminariaceae, Alariaceae, and Dictyotaceae have studied to identify antidiabetic compounds.also different antidiabetic mechanisms of phlorotannins and some other bioactive compounds have investigated though the researches to determine the therapeutic agents that may have benefits for type 2 diabetes patients still required.

Keywords: Marine , antidiabetic drugs, brown algae

The necessity of folic acid intake in preventing neural tube defects, a systematic review (Review)

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Introduction: Neural tube defects (NTDs) are severe birth defects of the central nervous system that result from a failure of neural tube closure process. The global incidence of NTD varies between 1 and 10/1000 births. This variation is likely to indicate different contributions from risk factors such as folic acid deficiency, maternal diabetes and a high glycemic index diet. Folate is a key micronutrient needed for normal cellular function. The use of folic acid will effectively reduce NTD by public health measures before and during early pregnancy.

Methods: We searched the literature available in PubMed, Google scholar, Sciencedirect, SID and Magiran databases for English articles published between 2000 and 2020. For this purpose, we used the words Prevention-NTDs, NTD dietary improvement, Neural tube defects and folic acid deficiency and neural tube defects as keyphrases. Among 100 articles found, 20 were irrelevant then excluded and 80 related articles were used.

Results: In 1965 the first observation of a link between folate deficiency and NTDs was published. in 1984–1991 The Hungarian randomized controlled trial of periconceptional multivitamin supplementation containing folic acid (0.8 mg) showed a substantial reduction in the first incidence of NTDs. However, Folic acid deficiency does not cause NTD in mice when genetic predisposition is not present. Another important risk factor of NTD is maternal obesity. Infants of obese mothers are more likely to have NTDs than children of normal weight. Therefore, obesity is not affected by supplementation of folate.However, Some of NTDs are potentially folic acid resistant. This notion is established in NTD mouse models in which folic acid inhibits other genetic forms while others are resistant to folic acid.possible adjunct therapy used in animal studies is inositol, which is successful in preventing a significant proportion of spinal NTDs, for which folic acid is ineffective.

Conclusion: The results show that the consumption of folic acid can be effective in the first occurrence of NTD. However, the relationship between folic acid, genetic and environmental factors is not yet well understood. Such models provide an opportunity to explore potential risks and create new preventative therapies.

Keywords: NTD,Prevention,Improvement,Diet,Folic acid deficiency

The prevalence of the most important food allergies in different part of Iran (Review)

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Introduction: The prevalence of allergic diseases has been on the rise during the last decades. According to epidemiological documents, high concentration of exposure to food allergen has resulted in several adverse problems including respiratory diseases, allergic reaction and infections. The purpose of this study is to provide an extensive review of the prevalence of the most common food allergens and sensitivity of people to them in different parts, which is crucial for the prevention and treatment of allergic diseases.

Methods: All published papers regarding food allergy in Iran were gathered from different databases and a standard review was written based on available data.

Results: This review shows an increase in the percentage of allergy to milk, egg, soy, wheat, peanut, tree nuts, shellfish, and fish during the last decades. Nuts especially almond, walnut, peanut, and hazelnut were common food allergens in several studies in different parts of Iran. Food allergy varies from city to city of Iran depending on the variation in lifestyles, nutritional habits, ethnic diversities, geography, and other environmental conditions. For example allergy to grapes and melon is prevalent in Mashhad while the most common fruit allergies in Tabriz are banana and tomato, and, allergenic reactions in Bushehr are caused by shrimps. This is due to the differences in nourishment, hence the amount of exposure to allergenic foods in various parts of Iran. However, it seems that wheat, egg, and milk are the most allergenic food among Iranian people since these foods are very common among Iranian diets all over the country.

Conclusion: In conclusion, the geographical variations in the prevalence of food allergies are likely due to the amount of exposure to different allergenic foods as well as environmental factors. Therefore identifying allergenic foods in each area is necessary not only for warning patients to avoid them but also for easier diagnosing, prevention and management of food allergic progress, the possibility of performing immunotherapy as well as decreasing the cost and morbidity of therapeutic actions for allergic patients.

Keywords: food allergy, epidemiology, prevalence, risk factors, allergic disease

The relationship between level of physical activity with lipid profile and anthropometric indices in office employees (Research Paper)

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Introduction: Cardiovascular disease is the leading cause of death worldwide. Meanwhile, several studies have shown that the blood lipid levels and anthropometric indices can be used as predictors of these diseases. In fact, controlling these indicators is very important to increase the level of health of people. On the other hand, office employees spend a lot of their time in sedentary behaviors such as sitting. This can increase the risk of various diseases, including cardiovascular disease and premature death. As a result, identifying strategies to improve lipid profiles and anthropometric indices can play an effective role in increasing community health. So the aim of this study was to investigate the relationship between level of physical activity with lipid profile and anthropometric indices in office employees.

Methods: This descriptive study was performed in Tehran, Iran. In total 154 office employees (Just male) participated as samples study in this research. Blood samples (TC, TG, HDL-C, LDL-C and LDL-C to HDL-C ratio) were taken from the brachial vein in sitting position and fasting state. Then anthropometric indices including body mass index (BMI), waist circumferences (WC) and waist-hip ratio (WHR) were measured and recorded. Then level of physical activity was measured by International Physical Activity Questionnaire short form (IPAQ). All statistical analyses were conducted with "SPSS 21".

Results: There was a negative significant relationship between Intense physical activity with triglyceride ($P<0.016$), WHR ($P<0.009$) and BMI ($P<0.007$). There was no significant relationship between Moderate physical activity or Light physical activity with lipid profile and anthropometric indices.

Conclusion: According to the results of this study, it can be stated that the intensity of physical activity has a significant role in the adaptations of lipid profile and anthropometric indices. So, it is possible to reduce the incidence of many diseases in these people by creating suitable conditions such as providing sports facilities for employees and increasing the level of physical activity.

Keywords: HDL, LDL, Anthropometric indices

The relationship between midwifery assertiveness and labor outcomes in primiparous women (Research Paper)

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Introduction: Pregnancy is a natural process in women's lives, but Midwifery skills play an important role in maternal health. Midwives are frightened and stressed by the injury and by unknown and ambiguous judgments and legal complaints. One of the causes of midwives' job stress is due to traumas that occur during delivery for clients. Stress, time constraints, concerns about poor performance, and lack of experience are factors that put pressure on midwives to refuse to act on evidence. Assertiveness improve communication skills,self esteem and finally making decisions. Midwives need personal skills and develop coping skills to respond to stressful issues in order to respond to clients' needs. The purpose of this study was to determine the relationship between midwifery assertiveness and labor outcomes in primiparous women

Methods: This is a descriptive correlational study that was conducted in Mashhad maternity hospitals in 2016. The researcher first provided the midwife with the Bar On assertiveness Questionnaire and collected their information, then collected information on 120 first-term births, headaches, unilateral and non-abnormalities delivered by the attending midwives. Did. Information on the outcome of childbirth was collected by a researcher-provided checklist. Data were analyzed by SPSS 16 software. Mann-Whitney nonparametric test was used because the two variables were not normal.

Results: The results of the study showed that the score of assertiveness in midwives was 84.1± 36.0 . Between midwives' assertiveness and duration of first and second stage of labor (p = 0.084), abnormal heart rate pattern in first and second stage of labor (p = 0.072), use of oxytocin (p = 1), episiotomy There was no significant relationship between postpartum hemorrhage (p = 0.09) and excessive postpartum hemorrhage (p = 0.086). There was also no relationship between midwife assertiveness and first minute Apgar score, need for resuscitation, dystocia and emergency cesarean section.

Conclusion: The present study showed that there was no significant relationship between midwifery assertiveness and childbirth outcomes. Therefore, it is suggested that studies with more samples be conducted, examining other psychological skills, and even training them on midwives' performance.

Keywords: labor Outcome, Midwife, assertiveness, Primiparous

The relationship between midwifery problem solving skills and labor outcomes in primiparous women (Research Paper)

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1. MSc in Midwifery Care, Departement of Midwifery, Scool of Nursing, Sabzevar University of Medical Sciences, Sabzevar, Iran.

Introduction: : Pregnancy is a natural process in women's lives, but Midwifery skills play an important role in maternal health. Midwives are frightened and stressed by the injury and by unknown and ambiguous judgments and legal complaints. One of the causes of midwives' job stress is due to traumas that occur during delivery for clients. Stress, time constraints, concerns about poor performance, and lack of experience are factors that put pressure on midwives to refuse to act on evidence. Midwives need personal skills and develop coping skills to respond to stressful issues in order to respond to clients' needs. The purpose of this study was to determine the relationship between midwifery problem solving skills and labor outcomes in primiparous women.

Methods: This is a descriptive correlational study that was conducted in Mashhad maternity hospitals in 2016. The researcher first provided the midwife with the Bar On problem solving Questionnaire and collected their information, then collected information on 120 first-term births, headaches, unilateral and non-abnormalities delivered by the attending midwives. Did. Information on the outcome of childbirth was collected by a researcher-provided checklist. Data were analyzed by SPSS 16 software. Mann-Whitney nonparametric test was used because the two variables were not normal.

Results: : The results of the study showed that the score of problem solving in midwives was 85.1± 36.0 . Between midwives' problem solving skills and duration of first and second stage of labor (p = 0.086), abnormal heart rate pattern in first and second stage of labor (p = 0.075), use of oxytocin (p = 1), episiotomy There was no significant relationship between postpartum hemorrhage (p = 0.09) and excessive postpartum hemorrhage (p = 0.088). There was also no relationship between midwife problem solving skills and first minute Apgar score, need for resuscitation, dystocia and emergency cesarean section.

Conclusion: The present study showed that there was no significant relationship between midwifery problem solving skills and childbirth outcomes. Therefore, it is suggested that studies with more samples be conducted, examining other psychological skills, and even training them on midwives' performance

Keywords: labor Outcome, Midwife, problem solving skills, Primiparous

The role of adiponectin in increasing insulin resistance in women with polycystic ovary syndrome (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of childbearing age and the most common cause of infertility due to anovulation, which is associated with symptoms such as high insulin, elevated male or androgen hormones, and ovulation disorders. Insulin plays an important role in this disease and its high level in the blood of these patients may cause the body to become insulin resistant and cause diseases such as type 2 diabetes, hyperlipidemia, atherosclerosis and finally cardiovascular diseases. Insulin resistance can also play a major role in the pathogenicity of PCOS. Adipocytokines are biologically active molecules derived from adipose tissue cells. One of these adipocytokines is the hormone adiponectin. Recently, the hormone adiponectin has been identified as a substance with important metabolic effects that is involved in lipid metabolism and the mechanism of action of insulin. There is evidence that serum adiponectin levels are affected during obesity and insulin resistance. The aim of this study was to investigate the role of adiponectin in insulin resistance and polycystic ovary syndrome.

Methods: This review was performed within articles published at PubMed,Google scholar and SID from 2015 to 2020. the keywords were adiponectin,insulin resistance and polycystic ovary syndrome. by searching this database , 66 articles were found. The titles of 33 articles were not relevant to our research and 18 of them by reading abstract were removed. All articles were selected from English and Persian articles.

Results: Finally, 15 articles were included in our study. Eight articles definitively mentioned the association between decreased serum adiponectin levels and increased insulin resistance in women with polycystic ovary syndrome. Studies of 5 articles showed that serum adiponectin levels were low in women with PCOS. However, no significant relationship was found between adiponectin levels and insulin resistance. One of these articles, which was performed on 43 women with polycystic ovary syndrome and 39 healthy women, suggested that low adiponectin levels may be secondary to hyperinflation. Androgenemia (not due to insulin resistance).A cross-sectional study of 44 women with PCOS and 16 healthy women showed that insulin resistance and adiponectin levels were significantly higher in the female patient group. This increase can be considered as a useful

compensatory mechanism. In addition, evidence from one study showed that lean women with insulin resistance had lower serum levels of adiponectin than lean women without insulin resistance.

Conclusion: According to our study, there is a relationship between serum adiponectin levels and insulin resistance in PCOS women, but today adiponectin is studied more as a marker and not as a treatment option, so further study on its therapeutic aspect on PCOS Recommended. Also, since adiponectin is a marker of adipose tissue, measuring its serum level to measure insulin resistance in lean women may provide misleading evidence, so further studies in this area may be helpful.

Keywords: adiponectin , insulin resistance , polycystic ovary syndrome

The Role of biosensors for the detecting the novel SARS-CoV-2 virus (Review)

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Introduction: Diagnosis of active SARS-CoV-2 infection is the most crucial step for overcoming COVID-19 health emergency. In order to reach this the target a highly sensitive, quick, and affordable test is much in demand. Utilizing biosensors to diagnosis SARS-CoV-2 antigens can provide reliable, simple, rapid, low-cost detection platform.

Methods: the pubmed and scopus were searched with keyword of "SARS-CoV-2" or "COVID-19" and Biosensor then the related articles were selected.

Results: 1. A field-effect transistor (FET)-based biosensing device The FET-based sensor is based on an immobilized SARS-CoV-2 spike antibody onto the surface of the Graphene sensor via a probe linker. The Graphene has the ability to sense voltage changes due to SARS-CoV-2 antigen connection to the immobilized antibody and then the signal can be detected via a detector. This FET biosensor can detect the SARS-CoV-2 antigen at concentrations of 1 fg/mL in phosphate-buffered saline and 100 fg/mL in the clinical transport medium. Moreover, the FET biosensor could detect SARS-CoV-2 in culture medium (limit of detection [LOD]: 1.6 × 101 pfu/mL) as well as clinical samples (LOD: 2.42 × 102 copies/m)(1). 2. Dual-Functional Plasmonic Photothermal Biosensor Combination of the plasmonic photothermal (PPT) effect with localized surface plasmon resonance (LSPR) leads to production of a highly sensitive biosensor, that is able to select SARS-CoV-2 sequences specifically. the biosensor is based on two-dimensional gold nanoisland (AuNI) with immobilized complementary DNA receptor. This dual-functional Biosensor is able to detect RdRp-COVID, ORF1ab-COVID, and E genes from SARS-Cov-2 with a detection limit lower to the concentration of 0.22 pM therefore, provide accurate detection of the SARS-CoV-2 sequences in a multigene mixture. Similar sequences like RdRp sequence in both SARS-CoV and SARS-CoV-2 can be accurately distinguished as a result of the in situ PPT enhancement on the AuNI chips leads to more efficient hybridization kinetics and more specific nucleic acid detection(2). 3. Cell-Based Biosensor Sophie Mavrikou et al. reported a biosensor set up on membrane-engineered mammalian cells carrying the human chimeric spike S1 antibody. They demonstrated hyperpolarization of the engineered cell membrane as a result of interaction between the antibody-bearing membrane-engineered cells, and the SARS-CoV-2 leads to electrical changes in the cell membrane. Surprisingly, the results will achieved just whiten 3 minutes. Also, the limit of detection reported one fg/mL with a semi-linear range of responses between 10 fg and 1 g/mL (3).

Conclusion: Developing biosensors allows detecting SARS-CoV-2 antigen directly, which is a reliable indicator of the presence of active virus in an infected case. Overall, biosensors development provides simple, rapid, low-cost detection platform but, the need for mass production of the monoclonal antibodies and the complexity

as well as time-consuming process of its production, restrict the usage of biosensors in clinical diagnosis. However, biosensors can be a good alternative for RT-PCR and decrease pressure on PCR based detection methods.

Keywords: SARS-CoV-2 COVID-19 Biosensor

the role of nanomedicine ethics in biomedical researchers (Review)

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Introduction: Nanotechnology includes engineering, physics, biology, medicine, and chemistry, and uses these sciences to build new products. Nanotechnology research has recently intensified with the development of nanotechnology research in medicine, which attempts to provide drugs and therapies based on the principles governing nanotechnology for the purpose of human health and well-being. This study aims to identify the main ethical issues in nanotechnology in research.

Methods: In this review study, articles related to the search for the keywords "nanotechnology or nanomedicine", "bioethics or nanoethics" and "risk or safety" in academic databases were retrieved and analyzed.

Results: Ethical issues in the field of nanomedicine research that should be considered is a subset of ethical principles that are generally considered in biology, but due to the special properties of nanoparticles such as unknown side effects and their diversity, the focus of these principles is Highlights nanotechnology presuppositions. The most important ethical issues known include respect for autonomy, informed consent, privacy and confidentiality, lack of control over human ability, justice and access to the role of ethics in nanomedicine. Medical nanotechnology is the use of nanotechnology in the treatment, diagnosis, monitoring and control of biological systems and is primarily in clinical medicine and preclinical research.

Conclusion: Ethical principles in biological research should be implemented in all three stages of prevention, diagnosis and treatment to protect human volunteers who participate in the advancement of knowledge. Harmlessness emphasizes the principle that research results should not be threatening.This includes not only the human condition but also the protection of the environment and the health of other organisms. Caution is important due to the special properties of nanoparticles, because medical nanotechnology plays an effective role in the prevention, diagnosis and treatment of many serious diseases, and if exploited and test results, many people are saved from the risk of death.

Keywords: Nano Medicine; Nanotechnology Research; Bioethics

The role of nutritional factors in prevention of cancer: A systematic review (Review)

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Introduction: Introduction: With the increasing prevalence of cancer in worldwide and changes in cancer patterns, the role of preventive agents of this disease has been considered. Nutritional patterns play an important role in preventing cancer. Therefore, the present study was conducted with the aim of a systematic review of the role of nutritional factors in prevention of cancer.

Methods: Methods: The present study was conducted by systematic review. To access the content related to nutritional factors and cancer prevention, articles indexed in databases, Proquest, Science Direct, Pubmed, Scopus, Googlescholar, SID were used. Keywords including nutrition, cancer, diet and prevention were searched over 2000 to 2020. According to the defined criteria, finally 25 articles were reviewed in this study.

Results: Results:The role of nutritional factors in cancer prevention in each type of cancer was investigated. The results showed that very hot drinks and foods and alcohol intake increase the risk of cancers oral cavity, pharynx and esophagus. Also,fruits and vegetables reduce the risk of these cancers. Grilled meat, salted fish and alcohol intake increase the risk of stomach cancer and fresh fruits and vegetables, green tea, garlic, saffron, omega-3 such as fish, tomatoe, Black raspberries, walnuts, hazelnuts, red grapes, black tea, onions, berries reduce the risk of stomach cancer. In colorectal cancer, increase the consumption of fiber and reduce the consumption of processed meats, vitamins A, C and beta-carotene, calcium, whole grains reduce the risk and red meat more than 4 times a week, fried foods, high-fat diet, grilled foods, Smoked fish, salty meat and pickles increase the risk. Aflatoxin and alcohol intake are related diet factors for liver cancer. Also, coffee reduces the risk of liver cancer. Some studies show that the risk of pancreatic cancer increases with high consumption of meat and decreases with vegetables. Although smoking is a major cause of lung cancer, studies have shown that low intake of vitamin A, fruits, vegetables and beta-carotene are involved in lung cancer. The only risk factor for breast cancer is alcohol. Fruits, vegetables and nutrients such as carotenoids and folate reduce the risk of cervical cancer. In total, fat, alcohol, salt, foods containing nitrate and nitrite, high-caloy foods high risk of cancer and high fiber, fresh vegetables, carotenoids such as tomatoes, vitamins C, E and selenium, legumes, carrots, broccoli , Sweet potatoes, pumpkin oil and pumpkin seeds reduce the risk of cancer.

Conclusion: Conclusions: Evidence for the crucial role of nutrition in cancer suggests that approximately 35% of cancer deaths are reduced with proper diet. Therefore, it is necessary to take measures to correct dietary patterns in order to prevent cancer. The Cancer Prevention Association has made recommendations to

improve diet and prevent cancer, including diversifying meals, emphasizing the consumption of whole grains, breads and cereals, fruits and vegetables, eating low-calorie foods, and limiting salt intake and Alcohol. Therefore, health policy makers should design and implement careful planning in this regard to change dietary patterns in families.

Keywords: Nutrition, Cancer, Diet, Prevention

The role of PI3K/Akt pathway platelet in cardiovascular disease (Review)

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Introduction: PI3K(phosphatidylinositol 3 kinases)are lipid kinase that generates intracellularly phosphorylated phosphoinositide.PI3K/Akt pathway interacts with proteins for signal transduction, vesicle trafficking and cytoskeletal reorganization. This pathway has a critical role in platelet activation and thrombosis formation.PI3K enzymes at three classes and eight-core isoforms indicate extensive-expression and broad function in mammalian tissues. Cardiovascular diseases are the first causes of mortality and morbidity in all over the world. The main reason for death due to CVD is an ischemic stroke or MI for which arterial thrombosis is a key part.

Methods: Published articles were reviewed if published in the scientific literature between 2000 and 2020. Searches were conducted using Pub Med, Scopus and Google scholar databases. Search terms included MeSH term," PI3K platelet", Cardiovascular disease" and "PI3K inhibitor".

Results: Platelets display an essential role in hemostasis, arterial thrombosis formation, prevention of hemorrhage and support repair at the vascular injury. However, when platelet hyperactivated, they result in arterial thrombosis and subsequently stroke or MI. Inhibition PI3K/Akt pathway in platelet prevents their activation and thrombosis formation accordingly MI doesn't occur.

Conclusion: Hence, they considered novel anti-thrombotic (PI3K inhibitors) that contrary antiplatelet drugs(ASA, Plavix) don't prolong bleeding time.This review will discuss the evaluation of role PI3K/Akt signalling pathway in cardiovascular disease.

Keywords: PI3k/Akt pathway, platelet activation, cardiovascular disease, PI3k inhibitor, Thrombos formation

The Steroid Receptors Gene Expression Possibly related to Serum Adipocytokines in Breast Cancer Patients (Research Paper)

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Introduction: The role of adipocyte-derived hormones in breast cancer pathogenesis well studied, it is speculated that there is a crosstalk between adipocytokines and Estrogen receptor(ER) signaling. To test this hypothesis we evaluate the possible correlation between serum levels of adipocytokines with steroid hormone receptors gene expression in breast cancer patients.

Methods: In this case-control study, 70 women with breast cancer participated with different grades of obesity (36 none obese, BMI < 25 kg/m2 and 34 obese, BMI ≥ 25 kg/m2). Serum level of adiponectin, leptin, TNFα, and IL6 determined by ELISA. Following the quantitative expression of the androgen receptor (AR), progesterone receptor (PR) and estrogen receptors (ERα and ERβ) mRNA in tumor tissues evaluated by Real-time PCR.

Results: A significant reverse correlation found between serum level of Adiponectin and ERα and PR mRNA ($r = –0.229$, $n = 64$, $p = 0.035$ and $r = –0.220$, $n = 64$, $p = 0.041$) but no correlation was between adiponectin and, ERβ and AR in samples ($P > 0.05$). In case of leptin, we observed a positive correlation between leptin and ERα and PR mRNA. ($r = 0.553$, $n = 64$, $p < 0.001$, $r = 0.359$, $n = 64$, $p = 0.002$ and a reverse significant correlation between leptin and ERβ ($r= –0.506$, $n = 64$ and $p < 0.001$). We also observed a significant correlation between TNFα and IL6 with steroid receptors gene expression in samples ($P < 0.05$).

Conclusion: As the presence of steroid receptors are used as the most common prognostic markers in breast cancer patients, so targeting adipocytokines as potential regulators of steroid receptorsgene expression can be a new approach in treatment of obese breast cancer subjects.

Keywords: Breast Cancer, Obesity, Adipocytokines, Steroid Receptors, Real-time PCR.

The study of effects Propolis extract on Beta-catenin gene expression in Gastric Adenoma Caesinoma cell line AGS (Research Paper)

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Introduction: Gastric cancer is a multifactorial disease. One of the environmental risk factors involved in the development of gastric cancer is the role of Helicobacter pylori infection. β-catenin is a dual protein in humans encoded by the CTNNB1 gene and is involved in the regulation and coordination of cell adhesion and transcription. The aim of this study was to investigate the effect of anti-cancer properties of bee propolis extract on β-catenin gene expression on AGS cell line.

Methods: First, bee propolis was extracted and the materials used in the cell culture process were aliquoted. Then, trypsinization of AGS cells with bee propolis extract at concentrations (800 and 1200 µg / ml) in 72 hours, RNA extraction, Cdna synthesis and finally Real Time PCR and statistical data analysis were performed, respectively.

Results: The studies performed in this study showed that the β-catenin gene had a significant increase in concentrations (800 and 1200 µg / ml) over a period of 72 hours, with the highest increase being related to the concentration (1200 µg / ml). It was statistically significant.

Conclusion: : According to these results, β-catenin gene under a period of 72 hours under the influence of bee propolis extract showed a significant increase and affected the progression of AGS cells to cell death and these results can be used by knowledge-based companies to produce The drug with bee propolis extract in appropriate concentrations to improve and control the progression of the disease in patients with gastric cancer.

Keywords: : β-catenin, AGS cells, bee propolis

Therapeutic Effect of Hemoderivative Materials in Regenerative Medicine (Review)

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Introduction: Nowadays, in many diseases, regenerative methods are used instead of palliative and restorative therapies. Activation of a reparative cascade is the main physiological response of the body against damaged tissue which is controlled at the cellular level and regulated by bioactive plasma proteins, growth factors, and blood cells or other tissues. Tissue regeneration also proceeds through the inflammatory or exudative, proliferative, and remodeling phases. Hemoderivative materials are used for regenerative medicine which contain blood cells, growth factors, and proteins involved in wound healing. Regardless of the preparation method, use and maintenance of these blood products have some disadvantages and advantages. Used hemoderivative materials in regenerative medicine include platelet-rich plasma (PRP), platelet gel (PG), Platelet-rich fibrin (PRF), and platelet lysate (PL). Autologous conditioned serum (ACS) is a hemoderivative material with anti-inflammatory properties, helping wound and tissue repaired.

Methods: In this review, the last two decades published studies regarding the hemoderivative materials, preparation methods, its compounds and their application in regenerative medicine, tissue engineering and various diseases treatment including type 2 diabetes mellitus, knee injury, cutaneous wound healing, and bone regenaration were studied.

Results: Hemoderivative materials with anti-inflammatory cytokines may help passing the inflammatory phase and enter the wound and tissue healing phase. Additionally, this material contributes in migration, growth and cell proliferation via its growth factors and causes wound healing and damaged nerve tissue repair.

Conclusion: Hemoderivative materials can be considered to treat various wounds and tissue damage such as diabetic foot ulcers because of their different levels of growth factors and anti-inflammatory cytokines.

Keywords: Hemoderivative materials, Blood-derived product, Regenerative Medicine, Growth Factor

Therapeutic effects of young plasma injection on the brain of the elderly (Review)

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Introduction: Aging is the main cause of the most common human diseases. From about a decade ago to today, the Parabiosis method has become a useful method for studying the effect of an animal's age on its health. In this method, a young mouse shares its circulatory system with an old mouse. Sometime later, experiments showed that the blood of young mice in old mice had a rejuvenating effect, while the blood of older mice in young mice had a bad effect. New vascular networks have shown improvement in neuroinflammation as well as various age-related brain diseases, such as Alzheimer's (AD), Parkinson's (PD). Recently, significant efforts have been made to elucidate the positive effects of young plasma injection on the structure and neural function of the brain in mice and humans. And examine its limitations to determine prospects in this area. In this review we aim to investigate the Therapeutic effects of young plasma injection on the brain of the elderly.

Methods: In this review, we include an article that discusses young blood plasma on Brain tissue rejuvenation. All articles were published between 2016_2020 and have ethical considerations. We searched PubMed and Google Scholar search engine with acute keywords “young blood plasma”, “Alzheimer's disease”, “brain rejuvenation”. Initially, 63 articles were found using this method. Then We excluded 38 articles from the study by considering abstract and used 25 articles in this review.

Results: In 10 articles, the effect of plasma injection of young mice on AD model mice was shown, which showed that injection of plasma of young mice on AD mice can restore the levels of synaptic and neural proteins, thus short-term memory, learning, spatial memory. And the hippocampus of older mice has a positive effect. A study was conducted to evaluate the safety and efficacy of fresh frozen plasma injection of young people (yFFP) in people with mild to moderate Alzheimer's (AD), which showed that yFFP is safe and improves mild to moderate AD. In 7 articles, the effect of plasma injection of young mice on the brain tissue of old mice was studied, and their results showed that plasma injection of young mice had a rejuvenating effect on the neural tissue of old mice. In one study, the effect of plasma injection in young people on the treatment of advanced supranuclear palsy (PSPRS) was investigated. The results of the study showed that injection of young plasma did not affect slowing the progression of the disease. In the other study, the effect of bone marrow transplantation from young to old mice was investigated. The results showed that bone marrow transplantation in young mice improves learning ability and memory in older mice by stabilizing synaptic connections and reducing microglial activation in the hippocampus. In 4 articles, the factors in the plasma of young people and their rejuvenating effects on tissues, especially brain nerve tissue

in the elderly were studied. Another study was performed to determine the safety, tolerability, and possibility of plasma injection in people with Parkinson's disease (PD) and showed that the injection of young frozen plasma in a small group with PD is safe and has therapeutic effects.

Conclusion: So far, studies have been conducted to elucidate the positive effects of youth plasma injection on brain function in mice and humans, which could be the first step in the development of drugs to treat diseases such as Alzheimer's and Parkinson's. However, the researches have been accompanied by limitations, such as the small sample size and short follow-up time. The results of larger clinical trials controlled with a double-blind placebo can make the results of these studies reliable if they have similar results. Further investigation is also needed for a dose, pharmacokinetic, and pharmacodynamic analysis.

Keywords: Alzheimer's disease, young blood plasma, brain rejuvenation, Parabiosis

Therapeutic use of microRNAs in NSCLC and SCLC. (Review)

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Introduction: The carcinoma of the lung is among the most prevalent types of cancer globally. With respect to its histology, it is divided into a non-small cell lung cancer (NSCLC) and as well as the small cell lung cancer (SCLC) subtype. NSCLC is the major types of lung cancer, which accounting for nearly 85 % of lung cancer. MiRNAs (miRNAs) are a class of non-coding RNA, which their nucleotides range from 19 to 25. They are known to be key regulators of cancer via epigenetic control of oncogenes expression, as well as the tumor suppressor genes. In addition, miRNAs albeit act differently in a lung tumor microenvironment, as they hinder the cell growth, and orchestrate apoptosis in the lung tumor cells. Here, this is a review on the roles of miRNAs for possible ways to prevent NSCLC and SCLC (anti – miRs, miR mimics and micro RNA sponges). Moreover we discuss new strategies to achieve tissue specific delivery, potential off-target effects, and safety of miRNAs delivery.

Methods: In this review we used online database such as NCBI (PubMed), Google scholar, and miRCancer Database. This Research is the result of a survey of more than 200 articles of which 115 articles are directly used in this study.

Results: The one of the main problems in the therapy of lung cancer are inappropriate methods of early detection and acquired medicine resistance which weaken the chemotherapeutic Advantages. Consequently, scientists want overcome this problem by discovering a new method with sensitive, accurate, and no side effects characteristic to treatment of lung cancer. MiRNA functions such as regulating protein expression during cellular activity, such as growth, development, and differentiation at the transcriptional, posttranscriptional, translational level, proliferation and apoptosis are essential in maintain the status quo of the cell. It also possesses less known side effects, and indeed an enhanced accuracy. However, weak infiltrates of miRNAs into the tumor tissue, unmodified miRNA antagonists, rapid degradation and clearance of miRNA mimics in blood circulation are led to shortcoming prevent and hinder the clinical efficacy of miRNA delivery. As result, it is necessary to treatment lung cancer (NSCLC and SCLC) utilized the suitable delivery strategy including lipid-based, polymer-based, scaffold-based, viral vectors and nanoparticles.

Conclusion: Further research on miRNAs such as effective delivery system of therapeutic miRNAs in inhibit SCLC and NSCLC, can certainly deepen our understanding of various malignancies lung cancer, and subsequently more effective treatment method. In general, miRNAs are effective and potential

therapeutic method to treatment of SCLC and NSCLC with less side effect and high accuracy.

Keywords: Lung cancer, MicroRNA, Treatment, Delivery system

Trace Elements of Copper and Zinc in saliva of patients with OSCC (Research Paper)

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Introduction: There are growing appeals for understanding the role of trace elements in oral squamous cell carcinoma (OSCC) diagnosis and tumor progression. The aim of this
study is the comparison of copper (Cu) and zinc (Zn) concentrations in saliva of patients with OSCC and healthy individuals and the comparison of these trace. elements among the patients with different histopathological grades and clinical stages of OSCC.

Methods: In this case-control study 30 patients with OSCC in different grades and stages and 30 healthy individuals as a control group were recruited. Unstimulated saliva of the participants was collected using spitting method. The Spectrophotometric Method was used to determine the salivary Cu and Zn and concentrations. Mann-Whitney test, Kruskal Wallis, T-test and ANOVA test were used to analyze the data. Significant differences were reported in p-values less than 0.05.

Results: There was a significant decrease in salivary level of Zn in the OSCC group in comparison to the control group ($p<0.05$). However, the salivary levels of Cu increased significantly for the same comparison ($p<0.05$). The different salivary levels of above elements among patients with well differentiation, well to moderate and moderate OSCC were insignificant ($p>0.05$). There were no significant differences in salivary levels of Cu and Zn between patients with first, second and third clinical stage ($p>0.05$).

Conclusion: This study indicated the salivary Cu and Zn alterations in newly diagnosed patients with OSCC. however, the role of these elements in tumor progression is still unclear. Overall these findings are in accordance with findings reported by Balpande et al. Also our findings are similar to Carausu et al. 2016 who found a significant increase in levels of Cu and decrease in levels of Zn in saliva and serum of 35 patients with oral cancer in comparison to the control group. Understanding the changes in metabolism of Cu and Zn occurring in the oral epithelium cells of tumor can be an orientation toward finding new diagnostic/prognostic biomarkers or a new intervention for prevention/ treatment of OSCC.

Keywords: OSCC, Zinc, Copper, saliva

Treatment of cancer using bacteria and their products (Review)

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Introduction: Cancer is one of the deadliest diseases in the world [1]. Bacteria and their spores, because they are selective for tumor tissues, also act as ideal vectors for delivering therapeutic proteins to tumors. Bacterial toxins have also emerged as promising cancer treatment strategies. The most promising strategy is prodrug enzyme therapy using genes. Although it has shown successful results in vivo, more research is needed on the mechanisms by which bacteria are targeted to develop a comprehensive therapeutic approach to cancer treatment [2].

Methods: An important factor that applies to the regression of cancer is the duality of the immune system [3]. Bacteria interact with the host as either pathogen or normal flora. The pathogenic interaction of bacteria enhances the immune system of the host in different ways [4]. certain bacteria have tumor finding nature defined as the ability to replicate inside tumor cells preferentially where the intracellular bacteria may evade host immunity. These approaches with bacteria so far have relied mostly on host immunity to indirectly impair cancer cells [5]. The production of pro-inflammatory cytokines such as IL-1β by lipopolysaccharides secreted by bacteria such as Salmonella typhimurium can damage cancer cells [4]. The fundamental advantage of bacteria-based cancer therapy is the capability to specifically target tumors via unique mechanisms. The use of Streptococcus pyogenes OK-432 in the successful treatment of sarcoma has shown promising results for the use of this bacterium in the treatment of lymphangiomas in children [6,7]. Bacterial toxins work by killing cells and altering the cellular processes that control the proliferation, apoptosis and differentiation associated with cancer. Another form of bacterial usage is spore, which are highly resistant bacterial forms. Other bacteria are used in the form of DNA vaccines, which stimulate the immune system against cancer cells by presenting cancer antigens. Bacteria growing under competition and drug influence are highly likely to evolve new phenotypes against cancer. the formed biofilm and the bacterial proteins are the products of the SOS response triggered by anti-proliferative drugs, such as hydroxyurea [8] that is an antiproliferative drug for tumor treatment, induces multicellularity of P. aeruginosa via impairing planktonic proliferation. Polysaccharides from Streptococcus agalactiae inhibit adhesion of cancer cells to endothelial cells—an essential step in cancer metastasis [1]. Salmonella, Clostridium and Bifidobacterium have been shown to control tumor growth and promote survival in animal models. However, Clostridium and Bifidobacterium are obligate anaerobes which limits their growth to the necrotic region of tumor and thus limits their effectiveness. In contrast, Salmonella is a facultative anaerobe which can grow in the viable as well as necrotic regions of tumors giving it greater potential as an anti-tumor agent. The S. typhimurium A1-R mutant, which is auxotrophic for Leu-Arg, has high anti-tumor virulence. In vitro, A1-R infects tumor cells and causes nuclear destruction. A1-R was initially used to treat metastatic human prostate and breast tumors that had been orthotopically implanted in nude mice. Substrains with tumor specific promoters and mutants which enhance selective tumor targeting have been

identified [9,10]. Bacterial enzymes are one of the most important products of bacteria in the treatment of tumors. Bacteria such as Escherichia coli, Pseudomonas acidovorans, Beauveria bassiana, Acinetobacter can be used in the production of drugs as antitumors by producing enzymes such as L-asparaginase and L-glutaminase, L-tyrosinase, galactosidase [11]. L-asparaginase is among the main drugs used for the treatment of acute lymphoblastic leukemia and certain non-Hodgkin lymphoma. L-asparaginase has been isolated from various sources including bacteria, algae, fungi, plant and mammals. Currently, native asparaginase obtained from E. coli and Erwinia chrysanthemi are most frequently used for treatment of ALL [7,11].

Results: To enhance the positive consequences of bacterial cancer therapy, the usefulness of eukaryotic and prokaryotic expression systems for the delivery of therapeutic payloads, such as L-arabinose-inducible pBAD promoter, Acidosis-specific promoter, Quorum sensing and many others are used [12,13,14,15].

Conclusion: Anticancer therapy with the use of bacteria is often marginalized and neglected, But the positive effects of bacteria cannot be ignored. More studies are needed to investigate the clinical significance of cancer treatment and the beneficial properties of bacteria, but the findings so far show very promising results. Therefore, bacteria can be expected to be used with less harmful side effects in the treatment and control of cancer.

Keywords: Cancer, Treatment, Bacteria

Understanding of hsa-mir-363-3p role in breast cancer process by bioinformatics analysis (Research Paper)

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Introduction: Among the common malignancies, breast cancer assumes to have a high rank in the Females. according to the surveys it has been revealed that early diagnosis of breast cancer has a significant role in the inhibition of progression and development of breast cancer. moreover , it has been recognize that different factors could have impact on breast cancer diagnosis and treatment , such as micro-RNAs (small non-coding RNAs) and SNP(single nucleotide polymorphisms).according to the mentioned information , hsa-mir-363-3p , which is located on chromosome X , was selected for the further bioinformatics analysis.

Methods: To perform a wide range of bioinformatics analysis miRBase , miRTarbase , miRWalk , TargetScan , DIANA TOOLS, miRSNPdb, miRdSNP , miRNASNP , DAVID, GeneMANIA databases, GraphPad Prsim 8.0 , databases and R a programming language, were selected to obtain essential data about micoRNA basis , validated and predicted target genes , genes' expression , SNP , signaling pathways and genes' interaction network .

Results: The bioinformatics analysis of this survey has been revealed that has-mir-363-3p and its target genes named PIK3CD, PIK3R3, PIK3R1, NRAS of cAMP, ERBB, Focal adhesion and Regulating of actin cytoskeleton signaling pathways could affect the breast cancer process. Also, rs870266 in GPR85, a predicted target gene, have been recognized as a potential biomarker in breast cancer. Thus, further analysis in order to early diagnosis of breast cancer is highly recommended. In addition, genes' expression analysis via heatmap method, showed that PIK3R3 gene of hsa-mir-363-3p, probably assigns the largest difference in its expression among solid tissue normal and primary solid tumor, which remarks PIK3R3 as a potential target for the breast cancer early diagnosis.

Conclusion: Analysis of Focal adhesion, ERBB, cAMP and Regulation of actin cytoskeleton signaling pathways, showed cell proliferation, migration, invasion and angiogenesis processes in breast cancer via the activation of PIK3CD, PIK3R3, PIK3R1, NRAS which they are activated by a cascade of genes. Thus, the function prevention of the mentioned genes results in suppression of the pathways and noted the tumor suppressor role of hsa-mir-363-3p in breast cancer process. For the better understating of hsa-mir-363-3p role in breast cancer, the investigation of rs870266 role in this cancer, is needed.

Keywords: Bioinformatics, miRNA, SNP, Breast cancer, Signaling pathway

Use of microencapsulation to improve the stability of probiotics (Review)

Mahsa Heidari,[1] Mina Morovati,[2,*]

1.
2.

Introduction: Probiotics are living microorganisms that have many health benefits to the host after being consumed [1]. Many studies have emphasized the vital importance of probiotics to health, including increasing metabolism, relieve chronic intestinal inflammation, reducing infections, reducing allergies, reducing lactose intolerance, reducing serum cholesterol levels and having anti-carcinogenic, anti-mutagenic, anti-hypertensive activity and detoxifying several toxins such as aflatoxins in products [2-5]. Lactobacillus sp. and Bifidobacterium sp. are two kinds of probiotics mainly used in functional foods like dairy products [6]. Since these probiotics are very sensitive to processing and storage conditions as well as passing through the gastrointestinal tract, various methods have been proposed to maintain the survival, activity, and stability of probiotics and subsequently maintains their numerous properties. One of these methods is microencapsulation [7-9]. Microencapsulation (ME) involves the separation of active, sensitive, and unstable compounds such as antioxidants, unsaturated fats, vitamins, drugs, flavorings, amino acids, enzymes, living cells such as probiotics from the environment and protected them by a coating layer [10-14]. Benefits of microencapsulation of probiotics The viability of probiotics is affected by various factors such as pH changes like acidification in fermented products, mechanical stress, oxygen toxicity during production, packaging, transporting conditions, and digestive enzymes in the stomach [15-18]. Stabilization and encapsulation of bacteria can protect cells during fermentation and drying, protect against bacteriophage attack, and enhance cell survival in heating and freezing processes [18]. Coating materials One of the most common biopolymers used for microencapsulation of probiotics is alginate, which increases the survival of bacteria during the food production process and protects them from adverse environmental conditions [19]. In addition to alginates, other compounds used to encapsulate probiotics are carbohydrates (such as Gum Arabic, pectin, maltodextrin, modified starch, alginate, agarose, chitosan, pectin, cellulose, carrageenan), proteins, gelatin, and waxes [20-23]. Microencapsulation methods There are not many choices for microencapsulating living cells because bacteria and living cells are not heat resistant [18]. Extrusion, Coextrusion, spray-drying, freeze-drying, and vacuum drying methods are mostly used for microencapsulation of probiotics [24-26]. Other methods of microencapsulation of probiotics are spray-coating, emulsion, and spray-cooling/chilling [27]. Due to the importance of maintaining the function, non-interference in bacterial metabolism, and maintenance of functional ligands, more gentle methods such as extrusion that maintain function and even enhance bacterial function are recommended [20].

Methods: In this study, reviewing various articles on the methods of microencapsulation of probiotics, coating materials, and the benefits of microencapsulation of probiotics in food products, the most important and up-to-date information was collected and presented as a review article.

Results: The results suggest that microencapsulation can enhance the survival, maintenance, activity of probiotics in food products like dairy, fermentation products, etc.

Conclusion: Consumption of probiotics in foods, especially dairy products, is beneficial for human health. Because probiotics are very sensitive to adverse environmental conditions during food processing and storage, as well as after consumption in the internal conditions of the gastrointestinal tract, so many methods have been proposed to stabilize and maintain them. One of these methods is microencapsulation. Microencapsulation of probiotics is performed using various compounds as coating materials. Alginates, agarose, chitosan, pectin, cellulose gelatin, gums, fats, carrageenan are examples of compounds used as coating materials. Also, extrusion, Coextrusion, Spray-drying, freeze-drying, Spray-coating, emulsion, and Spray-cooling/chilling is some of the methods used to microencapsulate these living cells.

Keywords: Probiotics, Microencapsulation, Dairy products, Microencapsulation methods, Coating materials

Using Apelin and exercise to protect the cardiac cells: synergic effect in ischemia reperfusion injuries treatment in rats (Research Paper)

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Introduction: Apelin is an active endogenous peptide, which affects blood vessels. Also exercise increases angiogenesis after myocardial infarction and exerts cardio protective effects. The aim of the present study was to investigate the effect of Apelin and aerobic exercise on reducing the severity of Ischemia-reperfusion injury in rats.

Methods: The rats were divided into the following 4 groups 8 weeks before surgery (Langendorff model of perfusion): I) Ischemia-reperfusion (I/R), II: Exercise Ischemia- reperfusion (EX+I/R), III: Apelin+Ischemiareperfusion (APE+I/R) (Apelin 10 nmol/kg/day, i.p), and IV: Exercise+Apelin+Ischemia-reperfusion (EX+APE+I/R). Exercise was performed on a treadmill 8 weeks before the surgery at a speed of 17 m/ min for 10 to 50 min/day. The ventricular function was evaluated after I/R injury, histopathological and immunohistopathology indices were then measured at the scar tissue.

Results: The results of H&E, Masson's trichrome staining indicated that APE+EX pre-treatment reduced cardiac fi brosis and the percentage of collagen deposition. It also enhanced the microvessels density (MVD) and decreased the number of infl ammatory cells and apoptosis rate.

Conclusion: According to our study, Apelin and exercise preconditioning had anti-fi brotic and antiapoptotic effects on the ischemia-reperfusion myocardium cells, which could lead to the protection of cardiac cells

Keywords: ischemia-reperfusion, immunohistopathology, Masson's trichrome, pre-treatment, microvessels.

Using Bayesian Functional Principal Component and multi-nomial scalar-on-function regression with application in gene - data (Research Paper)

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Introduction: Functional Data analysis is a branch in statistics that considers the underlying curves for the observed data with dimension reduction methods. The high-dimensional dataset exists in any discipline such as bioinformatics. In this research, we introduce Bayesian functional principal component analyses and multi-nomial scalar-on-function regression by applying them with extensive simulation and a sample dataset.

Methods: We use functional principal component analysis with B-Spline basis functions and generalized cross-validation for smoothing them. We also consider prior distribution for eigenfunctions and estimate the posterior distribution and compare the results with the Winbugs and R. We also extend and use the Bayesian scalar-on-function regression to the multinomial responses for predicting the tumor type in the high-dimensional gene data. The sample dataset contains 63 subjects with 2308 gene expression measurements for four groups of small round blue cell tumors for tissue samples and extensive simulation.

Results: The minimum number of basis function to get the highest prediction accuracy for the model predictions were estimated. The overall accuracy, specificity, and sensitivity are 100%. We estimate the coefficient functions of each cell tumor type.

Conclusion: The high number of basis functions can model the underlying curves very precisely, but it takes time and increase complexity. We reach the same accuracy with the lower number of basis functions and smoothing parameters. The functional principle components are an efficient method for dimension reduction. We get the result with the extracted eigenfunctions and subject-specific scores in the regression.

Keywords: Biostatistics, Functional Data Analysis, Bayesian Data Analysis, Cancer

USING STEM CELLS IN THE TREATMENT OF NEORODEGENERATIVE DISEASES (Review)

Arezoo Montazeri,[1,*]

1. Shahed Mohandes Vakili

Introduction: Diseases that target the central nervous system and spinal cord are among the diseases which bring lots of pain and injury.it is estimated that the number of patients with neurodegenerative diseases is increasing, diseases that have not been cured so far. Therefore, finding ways to treat these diseases is crucial. The human nervous system is so complex and studing neurons in their natural place of their lives logically and morally is really hard. Stem cells have this ability to help to better understand of brain and nervous system and to overcome the obstacles in studing nervous system scientists can find some new ways for curing these types of diseases or just to alleviate the process of diseases spread.

Methods: The criteria of selecting=the criteria for selecting were the articles that contained information about stem cells and neurodegenerative diseases and how to use stem cells in treatment of these diseases Resources="stem cells for dummies “written by “Lawrence s.B.Goldsteim"and"Meg Schneider". "stem cells therapy in neurodegenerative diseases"from"ENZO". "stem cells for the treatment of neurodegenerative diseases written by “Elise dantuma","Stephanie Merchant"and"Kiminobu Sugaya" This article was written in less than a month .

Results: Alzheimer is one of the most common diseases of the dementia but it is diagnosed just after death. This special dementia starts with the destruction of synapses which are involved in memory learning and problem solving. Currently available drugs for treatment of AD are purely for symptoms. Most of the work currently being done focuses on some approaches. The first type of approach is based on the idea that amyloid plaques or the components that make these plaques are cause of all subsequent injuries.Therefore,if the plaque is removed, the disease can be prevented. Some trials are developing a vaccination strategy to remove plaques. The second approach is based on ideas about external factors that can cause or exacerbate Alzheimer. Lack of sufficient dopamine release is the most important cause of Parkinson’s diseases.PD itself is not fatal but complications from the disease can lead to death. Although medications such as"Levodopa"control many of the symptoms to some extent. The disease is incurable and progressive So far, scientists have had two major approaches to using stem cells or other cells to devise better treatment for Parkinson’s disease .one approach is to try to produce lab-derived neurons in the lab and transplant them to the black body or"striatum"to use for their normal function of supplying the dopamine required by the striatum. Marrow-derived mesenchymal stem cells(MSCs)have been proposed as a potential treatment for PD."Park “and colleagues investigated the use of MSCs in a PD mouse model to observe potential neuro-protective effect on neuronal loss.

Conclusion: New therapeutic strategies are being used in many clinical trials, they have significant limitations. Scientists are constantly having difficulty finding new

therapeutic solutions, for example, as one of the main approaches to Alzheimer's disease is the removal of amyloid plaques, but some people are partly responsible for the progression of the disease because it is not completely clear. Using stem cells in the laboratory is an interesting method because it can be examined whether transplantation of healthy cells into Alzheimer's mouse models can replace those cells with horseback cells or rescue damaged models. The use of stem cells is still very much in the experimental phase, but its use is a new way to see the miracle of this science in the treatment of diseases in the near future.

Keywords: STEM CELLS, NEURODEGENTAREATIVE, ALZHEIMER'S DISEASES, PARKINSON'S DISEASES

Uterine Protective Drugs in Cesarean section (Review)

Kimia alavian,[1,*]

1.

Introduction: Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide. The use of oxytocic drugs during THE cesarean section is an important intervention in the treatment of PPH. Numerous studies have shown that these agents have a narrow therapeutic range. Therefore, accurate knowledge by anesthesiologists about optimal doses and side effects is necessary. Due to the insensitivity of the receptors, second-line agents, e.g. prostaglandins and ergot alkaloids, may be necessary. In this review article, we check the hemodynamics and side effects of these drugs and propose a suitable dose for the limitations of postpartum hemorrhage.

Methods: This review article conducted in February 2020. includes articles were from four well-known databases, Scopus, Pub med, Google Scholar, and Web of Science. The articles that did not include the purpose of the article were excluded from the study.

Results: Oxytocin has numerous physiological effects such as contraction, sexual and maternal behaviors, cardiovascular regulation, memory stability, and the regulation of food and drink intake. It is the first choice of PPH. Major side effects of oxytocin on mothers are heart attack, arrhythmias, hypotension, nausea, vomiting, and headache. Because of the structural similarity with antidiuretic hormone (ADH), an overdose of oxytocin may cause water retention, hypertension, and coma. Due to the side effects of oxytocin, it is best to take the lowest effective dose possible in the most stable way. Oxytocin dose of 0.5 to 3 IU is believed to be appropriate in most cases. However, the dose and rate of intravenous oxytocin injection after and during delivery of the cesarean section is controversial. It was suggested that receptor desensitization may influence the effectiveness of oxytocin. Considering that repeated doses of oxytocin may become increasingly ineffective, second-line uterotonic factors are necessary. Carbetocin has a function similar to oxytocin that causes uterine contractions. It responds with a lower dose than oxytocin, but the side effects of carbetocin are similar to that of oxytocin. Ergot derived from the fungus, this alkaloid was the first effective oxytocic drug used to prevent and treat postpartum hemorrhage or abortion. Ergot causes a fast and sustained contraction of the uterus. The high prevalence of nausea and vomiting has led to its being excluded as a first-line of cesarean section agent. Prostaglandins (PGs) increase uterine contraction (like oxytocin). Side effects of PGs after pharmacological administration include fever, nausea, and vomiting. PG E1 is a widely available oxytocic which is less effective than oxytocin and ergot alkaloids. Oral consumption of PG E1 may decrease the need for additional uterotonic agents at the cesarean section.

Conclusion: Uterotonic drugs are fundamental intervention in the inhibition of uterine postpartum hemorrhage. Oxytocin is the uterotonic of first choice. Carbetocin and prostaglandins are second-line agents. Research into these drugs

with their narrow therapeutic range will improve our ability to limit postpartum hemorrhage during a cesarean section, while decreasing perilous maternal side effects.

Keywords: Oxytocin, Cesarean, Carbetocin, Prostaglandins

Utilization of Polydeoxyribonucleotide (PDRN) to Treat Ulcerative and Conjunctiva Cornea (Review)

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Introduction: Polydeoxyribonucleotide (PDRN) considered a biopolymer low molecular weight DNA consisting of a random deoxyribonucleotide arrangement. PDRN is generally extracted from sperm and trout's testicles (Oncorhynchus mykiss) and salmon (Oncorhynchus keta) with an extraction process to obtain over 95% purity. PDRN has been reported for binding with adenosine A2A receptors resulting in tissue regeneration, anti-inflammatory, collagen synthesis, the stimulation of cell migration and proliferation of specific cells such as endothelial cells, fibroblasts and osteoblasts. Activation of the adenosine receptor pathway has been represented to be effective in improving tissue remodeling and reducing the inflammatory response. Corneal conjunctival ulcers and damages recognized as one of the annoying eye disorders. The ulcer of the cornea is a withdrawal in the corneal epithelium which is a potentially serious risk for vision. The increasing amount of lens usage and lasic surgeries leads to micro damages, ulcerative disease of the cornea and conjunctiva from contact lens usage. Most of the preclinical and clinical studies on PDRNs regeneration attribute focused on skin, and only a few are about ophthalmic tissues. The present review aims to declare the advantages of PDRN in ophthalmic disorders.

Methods: Identifying the studies included in this review was performed with PubMed search strategy and following terms: "PDRN" OR "Polydeoxyribonucleotide" AND "Cornea" with the restrictions of publication year (between 1990 and 30th August 2020) and language (English). The included papers with the following eligibility criteria: studies containing PDRN extraction techniques, corneal tissue regeneration, PDNR pharmacological mechanisms and pharmaceutical products in the market.

Results: More than 30 studies were identified with our search strategy and finally, with performing another additional search 15 studies were selected. Based on the case-control studies re-epithelialization and wound healing with PDRN in the cornea were reported. Studies represent tissue repairing, increase in cell growth, proliferation and therapeutic angiogenesis. Moreover, PDRN counted as a source of energy and nutrition supply to the cornea. Also, the activation of the adenosine A2A receptor results in the anti-inflammatory effect of PDRN. One of the important determinants of PDRN's safety is the lack of effects on the immune system.

Conclusion: The wound healing and tissue repairing are PDRN unique features which make it a new advancement in the pharmacotherapy. In clinical trials, PDRN is considered as an ophthalmic therapeutic agent for the corneal epithelial wound caused by contact lens usage and ulcerative disease. Pharmacological properties of PDRN represent that in addition to stimulating the regenerative and healing

process of the corneal epithelium, it is considered as a source of metabolic energy for the corneal tissues to extend their physiological functions. The administration of PDRN eye drops about four times a day is well endured by patients during the re-epithelialization therefore it is essential to expand PDRN ophthalmic formulations, dosage forms and eye drops. Eye drops are more desirable for patients because of clinical proofs and evidence.

Keywords: Polydeoxyribonucleotide (PDRN), Corneal conjunctiva, Re-Epithelium

Validating a Persian Version of the International Consultation on the Nocturia Quality-of-Life questionnaire (ICIQ-NQOL) for Assessing nocturia among Iranian women (Research Paper)

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Introduction: : High prevalence of nocturia and its debilitating nature, addressing the quality of life of patients has always been a serious issue among researcher and health care providers in order to improve the quality of medical care. A few questionnaires have been translated or adapted to evaluate quality of life among those suffering nocturia. The present survey aimed to assess the reliability and validation of the Persian version of the International Consultation on Urinary Incontinence Short Form Questionnaire (ICIQ-NQOL) questionnaire among Iranian women suffering urinary incontinence

Methods: Translation of the Persian version of the ICIQ-NQOL was determined by native Persian and English speakers (including translation and back translation). The content validity was assessed by calculating content validity coefficient ratio (CVR), reliability by test-retest analysis and internal consistency by determining the Cronbach's alpha coefficient.

Results: Cronbach's alpha coefficient for ICIQ-NQOL questionnaire was 0.754, indicating a high level of internal consistency without redundancy. For the test–retest reliability analysis, the ICIQ-UI SF had a consistency coefficient of 0.795, indicating acceptable test–retest reliability. The clinical experts agreed that the questionnaires were intelligible and covered all important domains with an overall CVR of 0.93.

Conclusion: The Persian version of the ICIQ-NQOL has high reliability and acceptable validity to assess nocturia among Iranian women

Keywords: Nocturia Quality-of-Life questionnaire, Validation, nocturia

Versatile applications of recycled plastics (Review)

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Introduction: The statistics of plastic disposal in Iran is a highly visible environmental problem . Turning the recycled plastics into a hardy and porous plate pallet is a sustainable solution to eliminate plastic wastes damaging the environment. The large porous plastic plate pallet is made from recycled granulated plastics and viscous material and nanoparticles. This porous plate alone has the property of absorbing water. So if we install them as floor tiles around the swimming pools, they will absorb the spilled water over the floor ; Therefore the ground will no longer be slippery and it will be safe to walk on. Besides, if we place these plates in a rainy weather, the problem of muddy gardens is solved and the crossing will not be difficult. Another usage is about installing the plates with nanoparticles of sound insulation on the floor and the walls to prevent the passage of sound in the apartments . A further application is green walls . By installing these plates on exposed columns and walls in public places and adding seeds into the porous parts, these will turn into greenery surface with proper irrigation and maintenance. Then we will have a beautiful city with fresh air. In addition to all these benefits, this product has the great potential job opportunities for the job seekers and introduces great benefits in environmental protection. Both advantages of this product are signs of a sustainable developing country.

Methods: First , we should place some buckets in school for dividing plastic litters. After gathering and washing the litters made of plastics , it is the time for shredding the plastics in small pieces. Thirdly, it is needed to granule the plastics for the purpose of having the potential to be melted and to form it into different shapes. Another step is making small holes that is meant for the seeds we may put there to have green walls, or adding nano-particles designed for house's surfaces to reduce the noise pollution or many other related problems. Then it is possible to locate the plastics at the edge of swimming pools to protect people from falling down and when the sidewalk is muddy in a rainy weather ,it will not be difficult to cross .

Results: Due to the plastic's indestructibility, they have become an environmental threat. There are several ways to get rid of recycled waste. Owing to the population growth, the demands for plastic products has been increasing over the last 40 years. Among the methods of disposing of plastic wastes, recycling is only about 10 percent. This process reduces the consumption of oil and it's derivatives.

Conclusion: The usage of plastic is expected to increase in the future, so it is essential to raise it's recycling methods . Generally , this operation is done by recycling plastic wastes with other benefits. Firstly, while special bins for collecting plastic wastes are placed in public places, it will raise people's awareness about the dangers of plastics to the nature. Therefore, people will help protecting the environment by separating the waste for recycling. In this way, pollution of forests, beaches and seas will no longer occur . Via soundproof plastics , the apartments

with noise pollution problems will be changed to peaceful spots. Finally, we can mention the green walls that cause the beauty of the city, contribute to the mental and physical health of people.

Keywords: Plastic , nano-particles , environmental problem ,environment , recycling

Virtual clinics during the COVID-19 outbreak (Review)

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Introduction: During the COVID-19 outbreak, the provision of health services has faced challenges; face-to-face communication leads to increase the transmission of the disease, so many healthcare centers have provided only essential services. Virtual clinics could provide health care services for diagnostic, therapeutic, monitoring and consulting purposes through information and communication technologies. The significant results are reducing the transmission of coronavirus disease, workload, and costs. In addition, virtual clinics could improve the quality of services at any time and place in such circumstances. Therefore, this study aims to review developed virtual clinics during the COVID-19 outbreak.

Methods: In this review, a comprehensive search was done in September 2020 through PubMed, Scopus, and Google Scholar with the keywords of “SARS-CoV-2” and “Virtual clinic” alongside their synonyms in the titles and abstracts of the papers. At first duplicated and non-English papers were left out; then, the studies which were related to developing or evaluating of virtual clinics during COVD-19 outbreak were selected to extract information.

Results: The search resulted in 365 papers, among which 23 papers providing virtual clinics that designed during COVID-19 outbreak. They are developed in USA (10), UK (9), Canada (3), and Saudi Arabia (1). The virtual clinics provided health services in order to counseling and monitoring of patients with COVID-19 (3), cancer (2), diabetes (1), fractures and trauma (2), immunodeficiency (1), kidney stones (1), and also providing specialties such as maxillofacial surgery (2), men's health (1), dentistry (1), psychology and mental health (2), optometry (1), pediatrics (2), orthopedics (2), ENT (1), and Gastroenterology (1). Online visits were done through phone (17%), video conference (13%), or combination of them (61%). Moreover, patients and healthcare workers could communicate with each other through designed software, patient portals, e-mail, WhatsApp, and mobile applications. Some studies had addressed the challenges, flowcharts, and guidelines associated with implementing and running a virtual clinic.

Conclusion: Although the provision of health care is inevitable, it is also crucial to prevent unnecessary face-to-face visits during the COVID-19 pandemic. Therefore, using technologies to provide tele-health services could be a beneficial approach. The studies have shown that virtual clinics could facilitate communication between healthcare providers and patients in such circumstances and prevent unnecessary referrals to health centers. It also leads to improving the quality of care services and user satisfaction. Therefore, providing guidelines, frameworks, and software and

hardware requirements for the design and implementation of virtual clinics could be a priority for managers and decision makers.

Keywords: COVID-19, Pandemic, Telemedicine, Virtual clinic, Virtual visit

Virtual Evaluation of amino acids in of beta-lactamase SHV-1 active site and their reaction with penicillin G antibiotic (Research Paper)

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Introduction: Klebsiella pneumonia is known for as producing extended-spectrum beta-lactamase (ESBL) belonging to three families (TEM, SHV and CTX-M). Numerous studies have shown the high prevalence of integrons in ESBL-producing Klebsiella and their pivotal role in transmitting broad-spectrum resistance. They cause several types of infections in humans, including respiratory infections, urinary tract infections (UTIs), and bloodstream infections. Due to limited treatment options UTIs caused by antibiotic-resistant gram-negative bacteria are a growing concern. Resistance to β-lactam antibiotics is achieved by the hydrolysis of the β-lactam ring by β-lactamases. Resistance to some β-lactamses are inherent because the enzyme is encoded in the core genome of Kelebsiella pneumonia. SHV is constantly found on chromosomes and offers resistance to extended-spectrum of beta-lactame antibiotics such as ampicillin, tigecycline and piperacillin. The aim of this study was to investigate the active site amino acids of beta-lactamase enzyme involved in beta-lactam resistance.

Methods: The 3D structure of SHV-1 beta-lactamase enzyme was obtained from the protein data bank database (http://www.rcsb.org/pdb/home/home). Using molecular docking and AutoDock Vina software, the binding and reaction of the enzyme with the antibiotic penicillin G (CID: 590) was investigated.

Results: Molecular docking indicates the molecular basis of drug sensitivity. The most stable binding state of penicillin G to beta-lactamase had the lowest amount of free energy (-7.2 kcal/mol) which interacted with amino acid residues ASN170, ASN132, TYR105, VAL216 in active site of beta-lactamase.

Conclusion: With the advent of antibiotic resistance, it makes sense to look at the mechanisms of resistance because it can help decide which drugs are prescribed in different scenarios and ways to overcome them.

Keywords: Extended-spectrum beta-lactamase (ESBL), Molecular docking, Antibiotic resistance

Vitamin C supplementation during neonatal and juvenile period attenuated cardiovascular oxidative stress induced by hypothyroidism in rats (Research Paper)

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Introduction: Oxidative stress has been considered as a link between hypothyroidism and cardiovascular diseases. Vitamin C has been well known to have antioxidant effects. The objective of this study was to investigate the attenuating effects of vitamin C supplementation during neonatal and juvenile period on cardiovascular oxidative stress induced by hypothyroidism in rats.

Methods: Sixteen pregnant rats were used in the present study. After delivery, they were randomly divided into five groups (1) control group which received normal drinking water; (2) in the second group propylthiouracil (PTU) was added to drinking water to induce hypothyroidism; (3-5) in these groups PTU plus 10, 100 and 500 mg/kg vitamin C was added to drinking water. After lactation period, the offspring continued to receive the same experimental treatment for the first 8-weeks of their life. Seven male offspring of each group were randomly selected. Malondialdehyde (MDA) levels, total thiol concentration, the activities of superoxide dismutase (SOD), catalase (CAT) were evaluated in the aortic and cardiac tissues and also in serum.

Results: Thyroxin and total thiol concentrations and CAT and SOD activities were decreased while; MDA level was increased in serum, heart and aorta tissues of PTU treated animals. Additionally, treatment of the animals by vitamin C could significantly improve all of these oxidative stress parameters compared to the PTU group.

Conclusion: The results of this study demonstrated vitamin C supplementation during neonatal and juvenile period attenuated cardiovascular oxidative stress induced by hypothyroidism in rats.

Keywords: Vitamin C, Propylthiouracil, Hypothyroidism, Cardiovascular, Oxidative stress

Vitamin-B6 Effect on Decreasing the Risk of Pancreatic Cancer (Review)

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1.
2.

Introduction: Pancreatic cancer arises when cells in the pancreas begin to multiply out of control and form a mass. This tumor rarely occurs before the age of 40, and more than half of cases of pancreatic adenocarcinoma suffer over 70. Vitamin B6 is a B group essential vitamin which has been implicated in increasing or decreasing the expression of certain genes. Some of the important effects of vitamin B6 are transcription of glucocorticoids, gene expression of albumin mRNA, influence on expression of glycoprotein IIb by interacting with various transcription factors. As the result of this vitamin on expression of genes, we decided to review the effect of it on pancreatic cancer.

Methods: We conduct a comprehensive search in Medline and PubMed databases for trials, case-control and cohort studies.

Results: All the studies confirm that, Consumption of vitamin B6 in the higher quintiles reduced the risk of pancreatic cancer from 22% to 54% in different studies. The intervention in those taking vitamin B6 supplement could decrease the advantage of cancer by 42% and consumption with vitamin B6 + B9 together could decrease the cancer advantage by 76%. This vitamin may play a role in protecting DNA against oxidative damage and subsequent mutations and therefore can lower the risk of cancer.

Conclusion: Vitamin B6 intake could significantly reduce the risk of pancreatic cancer. The greatest effect of this intervention happen when vitamin B6 and B9 consumed together.

Keywords: pancreatic cancer, vitamin B6,vitamin B9

Wet Disc Testing of complex Mafenide acetate and cobalt Against Bacteria (Research Paper)

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Introduction: Today, due to increased infections, antimicrobial agents and coatings are necessary. Increasing bacterial resistance is attributed to drug abuse so that more potent antibiotics are needed. They also require topical disinfectant to reduce the occurrence of drug resistance. In addition to the development of antimicrobial agents, it is necessary to effectively inhibit the growth of microorganisms. Some materials such as Mafenide acetate and cobalt have many applications in industry and health because of having antibacterial properties. This study aimed to investigate the antimicrobial properties of Mafenide acetate and cobalt complex that have this property.

Methods: For this study, 0.1 mmol of mafenide acetate and 0.1 mmol of cobalt nitrate in 10 ml of ethanol solvent were refluxed for 3 hours. The reaction progress was monitored using thin-layer chromatography (TLC) in normal hexane: ethyl acetate tank in a ratio of (1: 4). The solvent was evaporated, and the precipitate was crystallized with 2-propanol solvent. In this study, the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of nanoparticles of zinc oxide were determined using well assay method.

Results: For each antimicrobial agent, the MIC and MIC were determined from the broth microdilution results and the mean zones of inhibition were calculated from the agar well diffusion. According to the results of this study, the MIC values of this complex for Staphylococcus aureus were 3% and the MBC values for Staphylococcus aureus were 6% concentration.

Conclusion: The present study showed that this complex can be used as a deterrent against the pathogens of the materials and avoid contamination. Finally, the results obtained in this study suggest that the use of this complex as an antibacterial agent in industry and health can successfully inhibit some of the most dangerous and frequent pathogens.

Keywords: Antibacterial, staphylococcus aureus, Microdilution,

What is breast cancer? (Review)

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1.

Introduction: Breast cancer is one of the oldest and most common diseases in women.Breast cancer is an exclusive disease of women, but men make up 1% of those affected.

Methods: Different reasons have been found for breast cancer.The main causes are: Having cancer in the past-Premature puberty-Childbirth over the age of 35-Premature menstruation-Infertility-Weight Gain-Excessive fat consumption-alcohol consumption-smoking-Menopause over the age of 55-Taking hormonal medications during menopause. Breast cancer also has some symptoms. Of course, the presence of these symptoms in a person's body can have other reasons. If you see these symptoms, you should see a specialist.The most common symptoms are: Breast skin changes (Like wrinkles, bumps, etc)-Breast size change-Deformation and discoloration of the nipple-Fluid secretion from the breast other than milk.

Results: Generally, breast cancer is can be prevented with a healthy lifestyle.The easiest prevention methods are: Exercise and balance weight-eating foods that contain vitamins E and C-eating fruits and vegetables-enough sleep-Avoid stress. Following these tips can greatly prevent breast cancer. To treat breast cancer, you must first diagnose whether the cancer mass is benign or malignant. For diagnosis, ultrasound, mammography, MRI, or biopsy are prescribed. Then specialist diagnoses that the breast should be completely removed or only the affected areas should be removed. If only the affected areas are removed, treatments such as chemotherapy, radiation therapy, or hormone therapy will be started. However, in some cases, breast tissue must be completely removed to prevent cancer cells from spreading to other parts of the body.

Conclusion: Nowadays, breast cancer is of particular importance because it is the most common type of cancer in women. It should be noted that women have formed the mainstay of the family as mothers, and also due to the fact that this disease affects women at the age when the individual has the highest social and personal productivity, so inform this is especially important for women.

Keywords: cancr breast breastcancer women

What is personalized medicine? (Review)

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Introduction: Personal medicine or personalized medicine means providing medical services (health, prevention, diagnosis, treatment and care) tailored to a person's genetics.

Methods: In this model, for example, the physician, aware of the information contained in the person's genome, can prescribe an effective drug (with minimal side effects) in the right dose and order the appropriate lifestyle changes and diet (Environment) to provide prevention and treatment of diseases and change traits. Therefore, this model of medicine can also be called genomic medicine. "Just as each person chooses the right shoe for their foot, the medical person who will be the new form of medicine in the future will allow the person to receive the medical service tailored to their genetics."

Results: From 2005 onwards, following advances in microwave technology, computer science, and statistics, it became possible to determine a person's genotype in all known mutations in a short time and at a low cost, and to create a genetic profile for the individual. And their pervasiveness is the basis of personal medicine, which allows a person to receive medical services commensurate with their genetics.

Conclusion: In summary, each person's genome can provide him or her with information about the following: Risk of disease Is a person carrying genes that may cause certain traits in their children? How does a person respond to medications, is he or she allergic to certain medications? Does a person's genetics make him or her prone to certain traits: lactose intolerance, adaptation to a particular diet, predisposition to certain sports activities

Keywords: personalized medicine